New Orleans Medical
and
Surgical Journal

Vol. 99 SEPTEMBER, 1946 No. 3

THE PHYSICIAN AS A WORLD CITIZEN*

RAYMOND B. ALLEN, M.D.
CHICAGO, ILL.

On important university occasions such as this, a university looks at its work and its relation to the society of which it is a vigorous, indeed essential, expression. Its greatest works, of course, are its scholarship, its science, its humane letters, but above all, its human products—the young men and women who have had the privilege of associating with great minds and skillful hands, the devoted men who have carried on the unbroken humanistic tradition of university learning and culture for more than a thousand years.

It is well to remind ourselves in this turbulent century that universities are among man's most durable institutions. Most of them have survived all the vicissitudes of life and of states. A. Lawrence Lowell remarked a few years ago that those which have disappeared did not die from attacks from without but died from within. Its strength and durability grow out of the university's vital intellectual ferment, its identity with the community and its needs, and at the same time its detachment and objectivity, its integrity of thought and purpose, and its selflessness. But most of all it is constantly renewed and renourished by the influx of new students with fresh points of view and inquiring minds.

Medicine has been part of this great tradition and has enriched all other university disciplines through its interest in health and disease, in human growth and development (intellectual and spiritual as well as physical), its interest in the natural sciences, the social sciences, and the humanities. It is well known that physicians of ancient Egypt and Greece, who laid the foundations for modern scientific medicine and its moral and ethical codes, were also among the first great naturalists and humanists.

In our time, however, the roots of medicine in the fundamental disciplines of the university seem to be farther and farther removed from the every day work of the clinic by the division of labor in medical teaching and practice among numerous basic and clinical specialties. This has taken place despite the recognition by medical schools for the importance of these disciplines as a preparation for medicine. Yet on closer examination one can see that the link between the clinic and the university in all of its aspects is very close indeed. Everyone is aware, for example, that the revolutionary advances in nuclear physics and chemistry have important implications for medical and biological studies generally. Wartime advances in medical science, great as these have been, will be insignificant compared with what lies ahead in our lifetime for all branches of science, including medicine. Today medicine is more firmly than ever rooted in its sister disciplines of

*Commencement address delivered at The Tulane University of Louisiana, School of Medicine, on May 15, 1946. A portion of this paper is paraphrased from the writer's monograph on "Medical Education and the Changing Order," published by the Commonwealth Fund under the auspices of the New York Acamemy of Medicine's Committee on Medicine and the Changing Order.

the university, not excluding the law and the other social sciences. A leader in legal medicine recently wrote: "Law will aid men of medicine and of science to extend the social effects of their discoveries, to eradicate certain maladies, to help cure the widespread disturbances of physical and mental health which now spring from socio-economic maladjustments. Between law and science the whole fabric of society may be spun anew."

Increasingly medicine has focused its attention on man as a social organism. We have a growing realization that, while there is still much to be learned about the physical aspects of the life of man, the great contributions of the future will come from the exploration of man's relationship to the society which makes him what he is and which he constantly attempts to mold to his desires. Justice Holmes put it more succinctly when he wrote: "Man, whether he realizes it or not, is always fighting for the kind of world he wants." In man's constant struggle to find happiness in an ever-changing technological world lies the challenge for any student of the future. Here if anywhere, in the ever new demands upon both society and the individual, will he find the answers to the many medical riddles that confront us today. Here perhaps he may begin to understand and help the suffering human beings in whom we can find no apparent physical reasons for suffering.

The study of medicine, therefore, must embrace the study of life in all its aspects, physical, psychological, and social. It is not suggested that the physician must be an expert in sociology, economics, law, business, personnel management and in countless other fields. It *is* suggested, however, that he should have a clear and comprehensive appreciation of the place of these aspects of society in the life of the individual. He should realize, for example, that preventive medicine is being practiced at a most effective level by the forward-looking businessman who takes an active interest in such things as employee nutrition, health services, housing, safety and recreation, as well as the cause of absenteeism, juvenile deliquency and other social problems. Likewise, the physician should recognize as an ally a government which attempts to remedy social, economic and industrial deficiencies and abuses. Such efforts will play a most important part in the doctor's struggle against those untoward environmental influences which make for occupational disease, maladjustment and degenerative changes in the individual.

"Society is indeed a contract . . . But the state ought not to be considered as nothing better than a partnership . . . to be taken up for a little temporary interest, and to be dissolved by the fancy of the parties . . . it is a partnership in all science; a partnership in every virtue, and in all perfection. And as the ends of such a partnership cannot be obtained in many generations, it becomes a partnership not only between those who are living, but between those who are living, those who are dead, and those who are to be born."—Edmund Burke.

Any well-educated and experienced physician realizes that the professional services of lawyers, ministers, teachers, social workers and personnel counselors are essential in supporting and helping the individual to make a successful adjustment to the conditions of a complex modern life. Imagine a society without one of these essential professional components. One sees at once that their friendly personal services, frequently offered without thought of financial gain, are the very keystones upon which society is built. This is something that can never he mechanized. Real professional service may have its technics, but, it cannot be a technology: It takes a man, not a machine, to understand a man. Useful as machines may be in making observations and recording man's reactions and actions, the information they provide is useless unless we have someone able to interpret it and make judgments on the basis of wisdom born of experience. Essentially, this is the function of the professional man, whether he be a physician, teacher, minister or lawyer. Out of the wisdom of his

life's experience he must make decisions and recommendations likely to help those who consult him. It is simply a case of the skilled and, therefore, the strong helping those who are relatively less fortunate. Knowledge and skill in the use of knowledge are power; they are the source of the authority and influence of professional men. The use of such power can be entrusted only to men and women of intelligence, character, and fidelity, for in them is the future wisdom of the race.

Medical education aims to produce physicians who are not merely skillful, but wise as well in the application of the art and science of medicine. To be wise, the physician must understand the physical and social setting in which his patients live. As a physician and a highly privileged citizen, he must encourage and participate in every community effort to improve living and working conditions for everyone. Thus he fulfills his obligation to attack disease and suffering at their sources and to remove as far as possible every aggravating cause of human disability.

The interest and enthusiasm of men in professional and business life are essential for community progress; but civic pride, vigor and leadership are derived from every phase of community life. The small and big businessman, banker, lawyer, engineer, druggist, doctor, minister, teacher, members of women's organizations, labor unions, chambers of commerce and governmental agencies, all contribute leadership to the public welfare. The doctor enjoys the respect of the community because of his learning and skill. He represents the viewpoint and detachment of science in the discussion of complicated health and community problems. If he can add the qualities of integrity, tolerance, fairness, kindness and friendliness, his influence for the good of the community will be beyond measure. In some backward areas, in fact, he may be the only person who exercises any influence for constructive leadership.

Most physicians who are attracted to community life are the kind of people who do not allow the technical and scientific character of their training to obscure their natural human approach to patients and fellow citizens. As the community demands more preventive medicine and gives greater and more serious attention to such evidences of social deficiency as poverty, unemployment, industrial strife, malnutrition, high rates of juvenile delinquency and illiteracy, the doctor will come to occupy an even more important place of social responsibility. Therefore, the doctor must prepare himself to fill this broader role of leadership. He must equip himself with a thorough understanding of the social, industrial and economic patterns of which he is a functioning part.

Now I should like to focus your attention for a moment upon a university's interest in the one great question which is of first importance for any thinking person today. This is the crisis between technology and the higher values in life and living for which men have been striving for centuries. The question is whether man has sufficient wisdom, humility, and social consciousness to use his newly-found powers for the constructive purposes of all mankind. Free men have proved that democracy, and our republican system of self-government particularly, has the inherent strength to be victorious in a world at war; they have yet to prove that they can win a durable peace. Never before has the intellectual, spiritual, and moral life of man faced a test of such a portent for good or evil. Medicine with its age-old concern for the sick, the poor as well as the rich, the weak as well as the strong, has been an influence for good surpassed only by the moral precepts of religion. The services of medicine, like those of religion, have been largely personal. There will always be need for personal services, but medicine of the future, if it is to progress as a social as well as a biological science, must broaden its outlook and adjust its educational program accordingly. Medicine is coming of age as a social science.

Thinking and planning for democracy must be bold and dynamic, drawing not only upon the talents of individuals, but

also upon the social discipline of the group. At times, unfortunately, our system falters. We have great difficulty in distributing evenly the goods and services, including medical services, that our expanding technology pours forth in ever greater abundance. Our social process lacks stability which, perhaps, is but a sign of growth and change. This should not be too alarming. But, when the system becomes so unstable that it upsets our relations with our neighbors and when we lack the self-discipline and social controls to resolve our differences rationally and peaceably, then just to this extent has education failed at one of its primary tasks.

College graduates generally fail to take an interest in legislation, state or federal, even when it intimately affects their own fields of business or professional activity. We have always maintained that training for leadership is a major function of a university. If this is true, then we are failing in our purpose when education does not develop in the individual a social and political consciousness to the same degree that it trains him for professional and vocational proficiency. If this is true, may it not also be that here is a significant reason for disharmony between government, that is, social controls within the framework of law, and the citizen who still believes that "that government is best which governs least"? Are our schools, at all levels, sufficiently conscious of their obligation to educate for responsible citizenship? This, I believe, is the most important question we must resolve if our Republic is to survive in the critical years through which we are passing.

But there is a larger question, one that concerns every American, whether he is a college man or not. It is: What has happened to our greatest national asset, the native American spirit; the selfless, Christian spirit that founded this great nation, that unified and preserved it from internal division, that industrialized a continent and that, twice in this century, joined with and led the peace-loving peoples of the earth in conquering tyranny and preserving our right to live as free men? To live for what? For the good life for all men everywhere? Or for the giddy life of getting and spending in which human values are overwhelmed and smothered by the petty value of material things? If the latter is our answer to a starved and war-torn world, if we demand an island of selfish American plenty within a world of want, then we are a dying nation with no hope of realizing our true inheritance of greatness. We are left, it seems to me, with only one choice; we must elect to bring the machine under social control; we must decide that economics should be made to serve the good life for everyone rather than merely that of a favored few; we must recognize that it takes a man, not an adding machine, to understand a man.

Time is short and apparently getting rapidly shorter. Universities must join hands with enlightened men everywhere, in the church, in business, industry, and labor, in the professions and in statecraft, to strive for the realization of our native American spirit and for greatness in the "brave new world" in which we live.

Universities must meet their obligation to the society from which they derive their right to exist. Today universities are meeting this obligation by adjusting their educational programs to emphasize, in equal measure, the development of social and political consciousness and training for proficiency in professional and technical skills. As medicine assumes its full stature as a social science, we may confidently expect the physician of the future to take his accustomed seat in the councils of community and state as a responsible and constructive citizen. To him the people may rightly look for leadership.

Medicine, like the peace, is indivisible. Its only concern is to advance its understanding of man, in health and disease, wherever on the face of this tortured planet he happens to live and to bring him as much relief from pain and disease as the knowledge and skills of the physician make possible.

Now may I congratulate this splendid

class upon its graduation from this distinguished and venerable University. Its pride in you, I trust, will equal your pride in being alumni of the Tulane University of Louisiana. This is an open door to the society of learned men everywhere in the world.

Thus today you as physicians have become world citizens, for learning, science, and medicine know no national boundaries. This is your heritage from the ages which I know you will cherish always. It is the gift of your University, a gift which I am sure you have richly earned.

Finally, speaking now as a physician, may I prescribe (with the permission of my friend, Dean Lapham, since I do not have a license to practice in Louisiana) a capsule of distilled wisdom for each of you. It is to be taken at your discretion as required by any circumstances in which you may find yourself. This prescription was first compounded by a great man of letters, Robert Walpole, who gave this advice to the young and I give it to you, the class of 1946: "Always good sense, good manners, good humor, and good faith." And may I add faith in yourselves, your country, your families, your fellowmen, and your God.

———o———

MIXED TUMORS OF THE PAROTID GLAND

J. D. MARTIN, M. D.
BATON ROUGE

Mixed tumors of the parotid gland are of complex structure. Microscopic examination usually reveals them to be of epithelial elements and mesoblastic tissues, chiefly cartilage, mucous tissue and cellular connective tissue. Any one of these elements may predominate, but usually all cell types are represented.[1]

These tumors may be found attached or lying in the substance of the gland and are noted on physical examination when they have attained a size sufficient to appear as nodules or masses in the area of the parotid gland or below or behind the ear and some seem to involve the aural cartilages. The predominating element of the tumor determines its consistency. Most of these tumors are firm and hard, but growths predominately cellular or glandular may be soft. On dissection the smaller tumors are usually found to be encapsulated, but in the larger tumors fusion with the connective tissue of the gland is noted.

These tumors are not rare. Stein and Geschicter[4] report an incident of one of every 208 persons out of 50,000 surgical patients seen; 17.4 per cent of this series were considered to be malignant. Boyd[10] reports 103 cases from the Mayo Clinic between 1912 and 1917 and 69 cases from Memorial Hospital, New York, between 1918 and 1921. Martin[2] reported on 65,351 patients admitted to Barnard Free Skin and Cancer Hospital during a 24-year period and stated that 70 exhibited mixed tumors, of which 34 were simple and 36 malignant mixed tumors. Martin's reported incidence is, I believe, an actual low because most of these tumors are seen and treated by general practitioners and general surgeons. Patey[3] reports that benign tumors are more common than malignant in a ratio of four to three.

Patient Before Operation

The incidence is higher in the white race (80.1 per cent) than in the negro race (19.9 per cent) in a ratio of four to one.[4] There is an almost even division as to sex and size of body.

Mixed tumors have been found in persons ranging in age from 11 months to 73 years.[1] The age of appearance has no bearing on the benignancy or malignancy.[7] The most frequent age of appearance, however, is in the third and fourth decade.[8]

Postoperative Appearance of Patient

Ewing[1] summarizes our knowledge of their origin as follows:

1. The endothelial origin has been disproved.

2. No single source of the mixed tumors meets all requirements.

3. The derivation of mucous tissue and cartilage from gland epithelium has been satisfactorily proved and there is no necessity of including in the originating tissue any cartilagenous structures.

Ewing therefore classifies these tumors under the heading of epithelial tumors.

Mixed tumors follow a fairly common clinical course. They may appear at any age, but most often in the third decade as a firm, hard, painless nodule in the parotid area, below or behind the ear or seemingly as part of the aural cartilage. There is a gradual increase in size over a period of many years. These tumors usually double their size about every five years or so.[7] Tom Spec Jones of Baton Rouge had a case of a 67-year-old white female with a mixed tumor of the parotid gland of 51 years' duration which was removed surgically. The tumor "was more than a foot long and measures more than 21 inches in circumference." The pathologist reported the weight of this tumor as nine pounds. The largest mixed tumor on record was one reported by Canterell in the Scottish Medical and Surgical Journal in 1907 which is said to have weighed 26 pounds.

Benign growths are characterized by their lack of pain and slow steady enlargement. Malignant growths enlarge more rapidly and patients with malignant tumors complain of severe pain radiating to the face, neck, jaw, ear and back of the ear, which pain is probably the result of pressure on the fifth nerve.[11] Ulceration is uncommon until growth is sufficient to interfere with circulation.

It is fairly generally conceded that malignancy is not a primary clinical entity, but rather a secondary change in these tumors. Boyd [10] and McFarland[7] report that excision fails in about 25-30 per cent of cases and Boyd[10] that recurrences are more common when the tumor is removed while small. Ewing[1] states that surgical removal is often followed by recurrences of increasing malignancy. Montanus[12] is of the opinion that there are no criteria which will enable one safely to predict for mixed tumors a benign course, local recurrence or distant metastasis.

Patients with benign mixed tumors live indefinitely; patients with malignant disease rarely live over two years after operation.

The present methods of treatment are: (1) A laissez-faire attitude; (2) surgical excision; (3) irradiation; (4) a combination of irradiation and surgery. The status of irradiation at present is a matter of con-

troversy, but apparently, except for palliation, it has not been effective.[2] However, the effect of preoperative irradiation seems to be beneficial to the surgeon in that it renders the capsule of the tumor tougher and less liable to rupture during operation.[3]

The important surgical-anatomical fact to remember is that the facial nerve emerges through the stylomastoid foramen and runs forward in the substance of the parotid gland. The nerve lies one inch deep to the midpoint of the anterior border of the mastoid process and a line drawn horizontally forward from that point to the posterior border of the ascending ramus of the mandible. As this nerve may be injured in the removal of benign tumors it is advisable to explain to the patient and to the family, preoperatively, that following surgery there may be great facial disfigurement as a result of section or paralysis of this nerve with resultant dribbling from the mouth, affected speech, impaired mastication, a blank stare to express all emotions and the weeping eye that cannot be closed.

The indications for surgery are: (1) The discomfort of the patient; (2) suspected or known malignancy of the tumor.

The predominant type of recurrence is local, but it may be to distant organs.

The differential diagnosis of these tumors is from: (1) Epidemic or infectious parotitis; (2) benign or malignant lymphadenopathy; (3) salivary calculus; (4) actinomycosis; (5) tumors of the jaw and antrum; (6) peritonsillar and buccal abcess.

CONCLUSION

It would appear that one should be in no hurry to treat these tumors, but should subject the patient to as long a period of observation as necessary to determine the rate of growth and possible malignancy of the tumor, more especially since malignant degeneration is many times more common following excision.

REFERENCES

1. Ewing, James.: Neoplastic Diseases, 4th ed. W. B. Saunders & Co., Philadelphia, 1942, 787-798.
2. Martin, Thomas M.: Treatment of tumor of the parotid gland, Arch. Surg., 36:136, 1938.
3. Patey, David H.: The treatment of mixed tumors of the parotid gland, Brit. J. Surg., 28:29, 1940.
4. Stein, Irwin, and Geschicter, C. F.: Tumors of the parotid gland, Arch. Surg., 28:493, 1934.
6. Greedman, A. O.: Mixed salivary tumor in the tonsillar region, Arch. Otolaryn., 4:14, 1926.
7. McFarland, Jos.: Tumors of parotid region, Surg. Gynec. & Obstet., 57:104, 1933.
8. Jackson, A. S.: Mixed tumors of the parotid gland, Wisconsin M. J., 31:696, 1932.
9. Livingston, S. K.: Teratoma of the right parotid gland with metastasis to sternum and second rib left. Am. J. Roentgenol., 44:887, 1940.
10. Boyd, P. L.: Mixed tumors of the parotid type, Am. J. Surg., 39:641, 1938.
11. Benedict, E. B., and Meigs, J. C.: Tumors of the parotid gland, Surg. Gynec. & Obstet., 51:626, 1930.
12. Montanus, W. P.: Mixed tumors of the parotid gland with metastasis, Surg., 4:423, 1938.
13. Shoas, M. M.: Preservation of the facial nerve in the excision of parotid tumors, U. S. Nav. Med. Bulletin, 27:351, 1929.
14. Personal Communication from Dr. Tom Spec Jones of Baton Rouge, Louisiana.

DISCUSSION

Dr. Tom Spec Jones (Baton Rouge): Dr. Martin has covered this subject in a thorough and interesting manner, and I have only one or two points of interest that may be added.

In my service we have had three of these massive mixed tumors of the parotid gland. All three were in white females past sixty years of age and all were on the left side. They weighed nine, six and four pounds respectively. It is my belief that tumors of the parotid are not common. The incidence given by many authorities varies within very wide limits. They are of the mixed-cell type, containing much connective tissue, and the cells are often imprisoned in cartilaginous and bony tissue, which is an effort at restraint by nature. When compressed between the fingers it has the feel of a tight cyst, but upon opening the capsule you find it composed of a mass of solid fibrous material.

There is usually no urgent need for haste in operating, and every effort should be made to determine, preoperatively, if there be any suggestion of maligancy, for of course that would determine the prognosis. For instance, a tumor which has been present, unchanged except for its gradual increase in size for a period of 40 or 50 years, is certainly not malignant.

There are four important facts to be kept in mind when you have decided upon operation.

1. Always warn the patient and family of the danger of injury to the facial nerve and its consequences.

2. Tumors of the parotid are not prone to become malignant, but, when they are, recurrence is quite likely to take place.

3. Radium and x-ray do not seem to have very much effect on the malignant gland.

4. Be careful not to injure the nerve. Remember, normally, it passes through the substance of the gland.

As a rule those tumors are painless and symptomless, except for the size and weight. In the largest of our series (nine pounds) most of the

weight was carried by an attachment of the capsule to the masseter and mastoid branch of the sterno-mastoid muscles. In addition, this lady had learned to support some of the weight by allowing it to rest on the shoulder, where she carried a permanent scar on the skin from the many years of pressure.

Because of the enormous size of those massive tumors and the consequent displacement and deformity of the ear, scalp and adjacent skin and soft parts, it is difficult to estimate the amount of skin to be removed. Make allowances for the postoperative atrophy of the skin and be certain not to remove too much.

SOME COMMON ERRORS IN FRACTURE TREATMENT*

LYON K. LOOMIS, M.D.†
NEW ORLEANS

The doctor who handles fractures can in some ways be compared to the driver of the automobile. The driver accepts the responsibility of guiding his automobile safely over the road to a successful destination; the doctor accepts the responsibility of guiding the fracture of his patient safely over a course of healing to a successful termination, namely the restoration of function in the injured part. Both the doctor and the driver usually realize their responsibilities and feel able to cope with them but despite their good intentions, unforseen accidents occasionally arise which always damage the automobile and sometimes injure the driver. It is only by a careful analysis of each individual accident that a disaster of the same type can be avoided in the future and the accident rate in general lowered.

A few of the common causes in fracture treatment are: (1) failure to trim adequately the cast in the palm of the hand in the treatment of Colles' fracture; (2) failure to include the elbow and wrist joints in the x-ray of any fracture of the shaft of the ulna; (3) failure to reduce accurately epiphyseal fractures about the elbow; (4) failure to reduce supracondylar fractures of the humerus as soon as possible after the injury; and (5) conservative treatment of long oblique or spiral fractures of the lower third of the shaft of the tibia.

Following reduction of the Colles' fracture, a plaster cast is usually applied either from the axilla to the metacarpophalangeal joints on the back of the hand or from the elbow to the metacarpophalangeal joints on the back of the hand. If care is not taken to trim the cast back to the palmar crease in the palm of the hand, a complete range of finger motion is difficult or impossible, and the patient many times develops permanent stiffness of the fingers from capsular contraction which occurs during the period of immobilization. Old people are particularly subject to such contraction due to the lack of elasticity in capsular tissues. If the mistake is made of enclosing the fingers of an old person in plaster for a period of weeks, permanent stiffness of the fingers may result. Such trouble can be avoided merely by trimming the cast back to the proximal palmar crease in the hand, thus allowing; (1) a complete range of finger motion while the fracture heals; (2) good tendon motion; (3) adequate circulation to the extremity because the patient constantly pumps a sufficient blood flow to and from the fracture site.

When a fracture in the shaft of the ulna is suspected or present, care should be taken to include both the elbow and the wrist joints in the diagnostic x-ray to make sure that there is no luxation at either the superior or inferior radio-ulnar joint. Frequently, fractures in the shaft of the ulna are accompanied by dislocation of the head of the radius at the superior radio-ulnar joint or dislocation at the inferior radio-ulnar joint. If the fracture is treated without an x-ray of the elbow and wrist joints, a dislocation may be found months after the injury, at which time the doctor must resort to surgery and the chances of a good functional result are poor. If the dislocation can be recognized at the time of injury, it can usually be reduced easily and such reduction also helps to correct position of the fracture of the ulna.

*Read before the sixty-sixth annual meeting of the Louisiana State Medical Society, Alexandria, May 6-8, 1946.

†From the Department of Orthopedics, Louisiana State University, School of Medicine.

The reduction of dislocated epiphyses of the elbow in the growing child cannot be overemphasized. When the epiphysis of the capitulum is displaced, it is usually rotated nearly 180 degrees by pull of the extensors of wrist and fingers. If it is not replaced accurately, growth on the radial side of the humerus cannot keep pace with growth on the normal ulnar side. Therefore, months or years after the injury, cubitus valgus will be noted due to diminished growth on the radial side of the humerus. In addition to this deformity, the patient may complain of weakness in the upper extremity or may present the symptoms and signs of ulnar nerve palsy due to gradual stretching of the ulnar nerve around the increased angle of the medial side of the elbow joint. When the epiphysis of the medial epicondyle of the humerus is displaced, the flexors of the fingers and wrist and the pronator teres tend to hold the fragment distally and sensory ulnar nerve involvement is sometimes apparent within a few hours or days after the injury. If the epiphysis is not accurately replaced, involvement of the ulnar nerve by gradual pressure of the epiphysis or by inclusion in the organizing hematoma may cause a delayed ulnar palsy appearing months after the injury.

When the doctor is presented with a recent supracondylar fracture of the humerus with much swelling about the wrist, it is frequently a temptation to put the patient to bed and place the arm in traction in the hope that the swelling will subside and the elbow can be reduced with more safety later on. This is not a rational approach to the problem. The more swelling of the elbow, the greater is the indication for immediate reduction. It is only by an accurate reduction of the supracondylar fracture that pressure upon arteries, veins, lymphatics and nerves can be relieved. It is only by removal of such pressure that normal vascular channels can be reestablished and good pulse volume returned to the hand along with relief of lymphostasis and venostasis about the elbow.

Long oblique or spiral fractures of the lower third of the shaft of the tibia when treated conservatively tend to heal slowly or result in non-union due to poor blood supply. If union does take place, shortening of the tibia frequently follows, which results in pelvic tilt and often back complaints years later. Both tendency for delayed union and shortening can be corrected by the relatively simple technic of open reduction and insertion of one or two vitalium screws across the fracture site. By this procedure the fracture is anatomically reduced, healing is accelerated by the hairline reduction, and normal length of the extremity is established. Of course, a 48-hour preparation should be adhered to before operation and after operation a high-leg cast with the knee in 135 degrees extension should be applied for the usual period of three to four months or until adequate healing is present.

—o—

A SYMPOSIUM ON SODIUM AND WATER BALANCE*

DISTRIBUTION OF POTASSIUM AND SODIUM IN BODY

FOSTER N. MARTIN, JR., M.D.†
NEW ORLEANS

The two important electrolytes of the body, from an osmotic standpoint, are potassium and sodium. They are present in solution in much higher concentration than other inorganic bases. For this reason they are also important in maintaining acid-base balance. In addition to these general effects they exert specific effects similarly to ions present in lower concentrations. They are so abundant in foods that deficiency of them is extremely difficult to produce in laboratory animals. They have, nevertheless, been shown to be essential.[1]

Changes in the amount or distribution of these ions produced by disease cause marked changes in the animal; for example, the high blood potassium in Addison's disease accounts for many of the symptoms[2] and the attacks of familial periodic paralysis, which are accompanied by low blood potassium, are relieved by administration

*Read before the New Orleans Academy of Science, April 26, 1946.

†From the Department of Pharmacology, Tulane University of Louisiana, School of Medicine.

of potassium salts.[3] In order to detect and evaluate such changes in the distribution of these ions, the normal distribution has been extensively studied. Such studies involve also the distribution of water, since the ions are present in solutions which are in osmotic balance. The information accumulated is still incomplete. The purpose of this paper is to present a scant summary of the available data on the distribution of these two elements.

DISTRIBUTION IN CELLS

The potassium of the body is almost entirely intracellular. This was shown by Macallum[4] who precipitated the potassium in sections of tissue by means of sodium cobaltinitrite. Microscopic examination then revealed the location of the potassium precipitated *in situ*. His results may be summed up by saying: (1) the intercellular spaces are practically free of potassium, (2) the nuclei of cells are free of potassium, and (3) the distribution of the potassium in the cytoplasm is characteristic for each tissue. For certain tissues this distribution was as follows: in nerve fibers the potassium is in the myelin sheath, concentrated at the nodes of Ranvier and in Frohmans rings, the axon is free of potassium; in the acini of the pancreas the potassium is most concentrated on the side of the cells toward the lumen; in cartilage the potassium is scattered in the cytoplasm, there is none in the matrix; in smooth muscle the potassium is located at the periphery of the cells; in voluntary muscle the potassium is located in the anisotropic bands.

Fenn[5] has questioned the distribution in muscle cells shown by Macallum. He says that the potassium should be distributed like cell water and that it is not likely that a solution twice isotonic would be present in juxtaposition to distilled water in the muscle cell.

Scott[6] had confirmed the distribution shown by Macallum through the use of a micro incineration technic. The ash patterns found showed bands corresponding to the anisotropic bands of the muscle. This ash made at 650°C. should contain the potassium which boils at 760°C. Though Macallum's results might be explained as a Liesegang phenomenon[7] provided the precipitant could enter the fiber only at the end such penetration of the cell is improbable. There is no similar explanation for Scott's results. It seems unlikely that two such different technics should produce the same artefact.

The location of cell sodium has not been worked out though there is some evidence that most of it may be present in a bound state.

DISTRIBUTION BETWEEN CELLS AND EXTRACELLULAR FLUID

The only tissue which can be separated readily into extracellular and cellular parts for direct analysis is the blood. In human blood the sodium is present for all practical

TABLE 1

POTASSIUM AND SODIUM IN BLOOD

m.M./L.H_2O

Animal	Serum (92% H_2O)			Cells (65% H_2O)			
	K	Na	K+Na	K+Na	K	Na	K/Na
Dog (9)	5.5	150	155.5	149.9	8.9	141	0.063
Dog (10)	....	.....	.....	144.0	.....	.....	.....
Cat (9)	6.0	156	162.0	148.5	8.5	140	0.060
Goat (9)	5.7	151	157.7	130.0	22.0	108	0.220
Sheep (9)	5.9	151	156.9	125.0	24.0	111	0.216
Cow (9)	5.9	152	157.9	124.7	23.7	111	0.213
Monkey (10)	....	.....	.....	159.0	.....	.....	.....
Man (9)	6.0	163	169.0	165.5	131.0	34.5	3.800
Man (8)	5.4	158	163.4	166.?	166.0	?	.....
Rabbit (9)	6.0	156	162.0	171.?	171.0	?	.....
Pig (9)	6.2	149	155.2	163.?	163.0	?	.....
Horse (9)	6.1	156	162.1	145.?	145.0	?	.....

TABLE 2

POTASSIUM AND SODIUM IN ADULT ORGANS

Organ	H_2O %	m. eq./Kg. K	Na	K/Na	K+Na	m. eq./L.H_2O K+Na
Muscle (8)	79	93	31	3.00	124	157
Skeleton (8)	44	16	79	0.20	95	208
Skin (8)	73	27	70	0.38	97	133
Brain (8)	90	85	75	1.13	165	183
Liver (8)	79	55	82	0.67	137	173
Intestine (8)	85	70	.....	.....	.....	.....
Lungs (8)	78	39	109	0.36	148	189
Kidney (8)	80	45	72	0.62	117	146
Heart (8)	77	64	80	0.80	144	187
Heart (11)	79	67.5	61	1.11	128	162
Pancreas (8)	80	58	38	1.53	96	120
Uterus (8)	....	37	65	0.58	102	.....

purposes exclusively in the plasma. If any at all is present in the cells it is a trace.[8] Earlier results shown in table 1 giving high cell Na[9] were probably due to contamination of the cells with plasma. In some other animals (notably the dog and cat) the sodium is in part in the cells. The erythrocyte sodium plus potassium in milliequivalents per liter of water is constant for all species, within the limits of error of the variations in analyst and methods, as one would expect, since the cell osmotic pressure is the same in mammals. The data shown in the table have been calculated, from the results given by the various authors, on the basis of milliequivalents per liter of water.

Even in the case of animals with a high erythrocyte sodium content, this element has been shown to be extracellular, with the exception of small amounts in muscle and larger amounts in the skeleton.[10]

TABLE 3

POTASSIUM AND SODIUM IN MUSCLE

Animal	H_2O %	m. eq./Kg. K	Na	K/Na	K+Na	m. eq./L.H_2O K+Na
Human, Adult (8)	79.0	93.0	31.0	3.00	124	157
Adult (11)	75.5	82.0	34.6	2.28	116	154
Monkey (10)	79.0	90.0	26.6	3.38	116	148
Pig (11)	72.9	65.0	68.0	0.95	133	176
Cow (11)	78.1	94.0	28.4	3.30	122	155
Steer (11)	79.8	68.5	45.5	1.50	134	168
Calf (11)	75.3	97.7	36.0	2.68	134	178
Deer (11)	75.2	86.0	30.6	2.70	117	156
Rabbit, thigh (11)	76.8	102.0	19.9	5.10	122	163
red muscle (11)	74.9	109.0	25.6	4.25	135	180
white muscle (11)	74.9	97.5	19.1	5.10	117	157
Rabbit (10)	80.0	78.0	29.0	2.68	101	127
Dog (10)	68.0	67.4	30.2	2.24	98	144
Dog I, thigh + back (11)	76.4	83.5	41.0	2.02	124	163
Dog II (11)	74.8	83.5	21.4	3.90	105	141
Cat, thigh + back (11)	75.1	98.0	31.8	3.08	130	173
Hen, breast + thigh (11)	69.3	119.0	41.5	2.86	160	203
Cock, red muscle (11)	75.4	95.5	33.5	2.86	129	171
white muscle (11)	73.1	105.0	33.8	3.11	139	190
Turkey, red muscle (11)	73.8	93.0	25.2	3.78	118	163
white muscle (11)	72.5	94.0	18.5	5.09	112	155
Frog, R. esculenta (11)	81.6	79.0	24.0	3.28	103	126
R. Catesbiana (11)	79.8	89.5	23.3	3.86	113	142

This tissue distribution has been determined indirectly. Chloride which is extracellular since cells are, for the most part, anion impermeable is used to calculate the amount of extracellular water in the tissue. Total tissue chloride/plasma cl. concentration=extracellular water. In tissues, with the exception of muscle and skeleton, the sodium present is accounted for by the extracellular water on the assumption that it has a sodium concentration like that of plasma. The excess sodium, above that accounted for by the "chloride space," in bone is not extractable with water or strong potassium hydroxide so is apparently bound in some way.

POTASSIUM AND SODIUM IN VARIOUS ORGANS

Since the potassium is intracellular and the sodium is extracellular and the two solutions are in osmotic equilibrium the K m. eq. per kg/Na m. eq. per kg. is the ratio intracellular water/ extracellular water. The K m. eq. per kg. + Na m. eq. per kg. is a measure of the total water content and K m. eq. per L. H_2O + Na m. eq. per L. H_2O is an indication of the part of the osmotic pressure accounted for by these two ions. Table 2 shows these relations for various adult human organs. The K/Na ratio is highest in the case of muscle and excluding the skeleton is lowest in the case of skin and lungs. The muscle then has about three times as much cell water as extracellular water while the skin and lungs have a reverse situation.

The electrolyte concentration of muscle has probably been studied more than that of any other tissue. Table 3 shows comparative data calculated from the literature. The variations shown here in K+Na are no greater than the variations reported for homologous muscles or even different parts of the same muscle. In general the K/Na ratio is high. The values given in the tables must be considered as average values rather than as fixed normals. There is considerable change in muscle electrolyte on contraction, with loss of potassium and gain of sodium by the cells. Loss of potassium during activity has been reported also to occur from heart muscle, nerve fibers and ganglia. Such changes probably occur in other organs during active functioning also. The one exception, which has been demonstrated, is the erythrocyte. Potassium cannot enter or leave the erythrocyte unless the cell is injured[12,13]. This injury is least in defibrinated blood, less in oxalated or citrated blood than in inorganic solutions and in inorganic solutions is roughly in proportion to their departure from average blood composition. The erythrocyte is anomalous also in that it is permeable to chloride.

POTASSIUM AND SODIUM OF WHOLE ANIMAL BODIES

Table 4 gives the potassium and sodium relations of whole bodies of various species.

TABLE 4
TOTAL BODY POTASSIUM AND SODIUM

Animal	H_2O	m. eq./Kg.				m. eq./L.H_2O
	%	K	Na	K/Na	K+Na	K+Na
Human, Fetus 5 mo. (8)	91	51	112	0.45	163	179
Fetus 6 mo. (8)	87	41	94	0.43	135	155
Fetus 7 mo. (8)	86	48	93	0.51	142	165
Premature 7 mo. (8)	85	44	105	0.42	149	176
Newborn (8)	80	49	78	0.63	127	159
Adult (8)	72	68	48	1.42	116	161
Monkey (10)	68	64	55	1.16	119	174
Dog (10)	59	48	55	0.88	103	175
Dog (14)	....	....	....	1.468	.....	.....
Cat 29 days (14)	....	....	.....	1.297	.....	.....
Rabbit (10)	74	63	48	1.31	111	148
Rabbit 14 days (14)	....	....	.....	0.835	.....	.....
Embryo (14)	....	....	.....	1.272	.....	.....
Mouse (14)	....	....	.....	0.787	.....	.....

The figures for the human show that the total water in the fetus is much higher (K plus Na per kg.) than in the adult and that much more of the body water of the fetus is extracellular (K/Na). In most adult animals the ratios are similar to those of the adult human. When the whole body is considered the excess sodium in the skeleton and muscle above that accounted for by the chloride space will introduce some error in the correspondence of the K/Na m.eq. per kg. ratio to intracellular water/extracellular water ratio.

The data from which these tables were calculated are in many instances inadequately stated for evaluation of their validity as standards. In many instances the number of animals was not stated, in some of these the analyses were apparently done on a single animal or single samples, so that in no case can these figures be accepted as absolute values but as averages or less.

BIBLIOGRAPHY

1. Orent-Keiles, Elsa, Robinson, Aaron, and McCollum, E. V.: The effects of sodium deprivation on the animal organism, Am. J. Physiol., 119:651, 1937.

2. Truszkowski, R., and Zwemer, R. L.: Corticoadrenal insufficiency and potassium metabolism, Biochem. J., 30:1345, 1936.

3. Pudenz, R. H., McIntosh, J. F., and McEachern, D.: The role of potassium in familial periodic paralysis, J. A. M. A., 111:2253, 1938.

4. Macallum, A. B.: On the distribution of potassium in animal and vegetable cells, J. Physiol., 32:95, 1905.

5. Fenn, W. O.: Electrolytes in muscle, Physiol. Rev., 16:450, 1936.

6. Scott, G. H.: Distribution of mineral ash in striated muscle cells, Proc. Soc. Exper. Biol. & Med., 29:349, 1932.

7. Gortner, R. A.: Outlines of Biochemistry, 2nd Ed., New York, John Wiley & Sons, Inc., 1938, p. 312.

8. Shohl, A. T.: Mineral Metabolism, New York, Reinhold Publishing Corporation, 1939.

9. Oppenheimer, Carl: Handbuch der Biochemie des Menschen und Tiere, Jena, Gustav Fischer, 1909, Vol. 1, p. 85.

10. Harrison, H. E., Darrow, D. C., and Yannet, H.: Total electrolyte content of animals and its probable relation to distribution of body water, J. Biol. Chem., 113:515, 1936.

11. Dische, Z.: Die anorganische Bestandteil des Muskels, Tabulae Biologicae, 3:446, 1936.

12. Davson, H.: Studies on permeability of erythrocytes: cation content of erythrocytes of rabbit's blood in hyper- and hypo-tonic sera, Biochem. J., 30:391, 1936.

13. Ponder, E.: Kinetics of hemolysis, Physiol. Rev., 16:19, 1936.

14. Roger, G. H., and Binet, Léon: Traité de Physiologie, Paris, Masson et Cie, 1:766, 1933.

BOUND WATER

L. MATTHEW N. BACH, Ph.D.†

The subject of bound water concerns itself with something about which there is so much doubt that it appears difficult even to attempt a definition. Bound water may be considered to be a synonym for water of hydration but it bears special reference to colloids, especially proteins; thus it concerns itself with water molecules which are combined with dissolved protein in such a way that the water becomes a part of the molecule kinetic unit of the protein. Under such circumstances this water is said not to retain its normal solvent properties nor does it participate to any extent in osmotic transfers so that it presumably possesses different physical properties than the surrounding free water.

It would seem necessary at least to note the complexity of structure of even free water. The molecular structure of liquid water is assumed to consist of hydrogen and oxygen atoms joined in the form of a "V" with oxygen at the juncture and H at each end. Further, these molecules are polymerized in varying numbers, either as dimers, trimers, or even higher polymers, the number of units depending upon such factors as the temperature and the types and concentrations of varius ions which may be present. X-ray diffraction studies show that, statistically the most common polymeric structure of liquid water is a tetrahedron consisting of four water molecules. At this point a quotation from an old chemistry textbook would seem appropriate: "Water is water, not a single substance in the proper acceptation of the term, but a mush or a mixture; an entirely peculiar substance, not to be represented by any single formula nor spoken of by any single name."

Many types of hydration are possible, ranging from simple mechanical entanglement to a closely packed dielectrically saturated water in an intense dielectric field. The degree and extent of controlling factors determining the type of hydration is im-

†From the Department of Physiology, Tulane University School of Medicine.

perfectly known. One well known example of hydration is the chemical combination of H_2O with NH_3 wherein a hydrogen bond is established between the N of the NH_3 and the O of the H_2O. But water combinations other than chemical bond formations involving the attraction of H_2O with other molecules are not well understood.

Necessary evidence for hydration in crystals is the presence of stochiometrical proportions of H_2O. A solid crystalline hydrate may not exist in solution, however, because solution breaks up the crystal structure. Furthermore, water does not take part in the crystalline structure apparently because during dehydration of a crystal, the structure is retained in the face of parallel increases in density and decreases in volume.

Possible means of hydration of a protein involve water combination by the formation of covalent bonds between water and the OH, COOH, NH_2, and NH groups of protein sidechains. These hydrophilic sidechains frequently serve as connecting links between polypeptide chains composing the protein molecule. Factors determining the extent of hydration of a protein molecule include the ratio of hydrophilic to hydrophobic sidechains, differences in ionic size, (especially great in the case of protein and water, thus tending to favor hydration) acidic or basic characteristics of sidechains which determine their efficacy as coordination centers for orientation of water dipoles, and finally, the isoelectric point where zwitterionic action may serve to approximate active protein groups thus preventing hydration by forcing out the solvating water. This latter point is illustrated in the case of gelatin at the isoelectric point where water imbibed during swelling retains its solvent properties and so is not hydrated or bound.

The binding of water by a protein is therefore easily visualized but is not so easy of proof. Several methods have been suggested for proving or disproving the presence of bound water, many of which depend upon the measurement of the colligative properties of bound and free water. The thermodynamic data thus obtained are reliable but their interpretation is open to doubt because of many complicating factors, not the least of which is the relation of water molecules to each other. The first of these methods involves adding a reference substance, such as sucrose or urea, to a gelatin solution and to a volume of water equal to that in the gelatin solution and then comparing the decrease in freezing points or in vapor pressures which should occur. If any water were bound by the gelatin, one should expect a greater decrease of vapor pressure or freezing point, but in actuality, no such difference has ever been observed since the freezing points and vapor pressures are lowered by the same amount in both solutions. This has also been found to be true for muscle tissue, blood, and egg white. A second method involves ultrafiltration wherein a reference substance such as glucose is added to a gelatin solution and this solution is then subjected to ultrafiltration, which should remove all water. This reference substance would be assumed to diffuse freely throughout the free water but not in the bound water. This experiment denies the presence of bound water, for the concentration of glucose in the ultrafiltrate is exactly the same as that in the original solution. A third method utilizes the separation of ice crystals following cooling of water. One would expect bound water not to freeze. It has been found with gelatin gel that a solid solution separates out at about -20° C. and the composition remains constant down to at least -45° C, with about 0.5 grams H_2O per gram of gelatin contained thus arguing for bound water. However, even as one of the most avid proponents of bound water admits, it takes a long time for equilibrium to be established between ice crystals and water—as long as 18 days—and these conditions are rarely observed. More importantly it is very probable that all of the water did not freeze out of the gelatin because it was supercooled and supercooled water will not ordinarily freeze

unless first seeded by ice crystals which, in this case, could not penetrate from the outside of the gelatin mass. A fourth method takes advantages of the property of birefringence which measures the regularity of positioning of protein chains and by its diminution, in the case of hydration, indicates disorientation of the molecular structure due to the presence of water molecules. Finally, x-ray diffraction pictures of hydrated proteins show an increased intramolecular spacing following hydration indicating the presence of water combined via the hydrogen bonds to the extent of about 0.4 gram H_2O per gram of protein. However these last two methods tell us only of the presence of water and not necessarily of the mode of combination or the nature of the combined water.

Accepted values (by those who believe in it) of protein-bound water vary from 0.2 gram H_2O to 0.5 gram H_2O per gram of protein but reported values range from 0.08 gram H_2O to 7 grams H_2O per gram of gelatin. The extent of hydration of proteins must therefore remain undecided and since the present trend of evidence indicates that there is little if any hydration of proteins for practical purposes all the water in protein solutions can be considered to be solvent water. There has been, as yet, no method developed to give precise information on the presence of bound water and we cannot be certain that water can form an integral part of the molecular-kinetic unit of intracellular colloids.

Certain practical aspects of bound water may be mentioned at this point, that is if there is any such thing as bound water. From x-ray data it appears quite certain that water is combined with protein and lipoid but whether this water is free or bound is uncertain. Let us then refer to this water as combined water which is probably not a better term but at least does not commit us to think of it as inactive water. One feature of such combined water occurs in the salting out effect of certain ions. These ions precipitate proteins by virtue of the fact that their affinity for water is greater than protein, and, by their presence, they dehydrate protein. Na and SO_4 are the physiologically important ions with the greatest affinity for water and Na_2SO_4 is one of the best protein precipitants. Another important role of combined water is in membrane structure. X-ray studies of myelinated nerves and erythrocytes show that these structures consist of bimolecular layers of lipoid which extend outward into a water layer on each side which separates one set of lipoid layers from its neighbor. When basic histone protein molecules are present, they may cause complete expulsion of the water layers by replacing them since they easily react with polar acid groups of the lipoid cephalin. Myelinated structures have been shown by histologists to possess channels communicating with the axis cylinder and although these might be fixative artefacts, they may also be correlated with water layers shown to exist by x-ray studies in brain lipoid mixtures. These spaces are found to vary according to the per cent of water in the solution. X-ray studies, interestingly enough, show the same degree and type of water layer disposition between molecules of cephalin-histone, thromboplastin, and blood platelets, indicating the structural relationship between these substances so important and similar in their actions in blood clotting. Finally, most germane to the general subject of the symposium, it has been shown, by x-ray studies, that the mitochondria of cells of the distal tubule of the amphibian kidney show a spacing between their lipoid-protein components of 42° Angstrom units in diffraction pictures. This relatively large spacing indicates a high degree of solvation of the polar groups of the lipoid and protein and may be important in the role of these cells in water transport from tubule lumen to tubule blood.

BIBLIOGRAPHY

Blanchard, K. C.: Water, free and bound, Cold Spring Harbor Symposium, 8:1, 1940.

Hober, R.: Physical Chemistry of Cells and Tissues, Blakiston, Philadelphia, 1945, section 5, p. 289.

Schmidt, C. L. A.: Chemistry of the Amino Acids and Proteins, C. C. Thomas, Springfield, Ill., 1938, chapter 9, section 7.

Schmitt, F. O., and Palmer, K. J.: X-ray diffraction studies of lipid and lipide, protein systems, Cold Spring Harbor Symposium, 8:94, 1940.

SODIUM AND POTASSIUM IN RELATION TO THE ACTION OF DIURETICS

RALPH G. SMITH, M.D.†
NEW ORLEANS

A complete discussion of the relation of sodium and potassium to the action of diuretics is impossible in the time available. Consequently the subject will be presented in the form of illustrations of the importance of the ions of these elements in diuretic action. Citations from the literature are chosen arbitrarily without attempting to make an extensive survey of pertinent publications.

SODIUM AND POTASSIUM SALTS AS DIURETICS

It is well established that there is a distinct difference between the behavior of sodium and of potassium salts with respect to their action as diuretics. Potassium has a much lower renal threshold than sodium. In other words after filtration through the glomerulus reabsorption by the tubules is much greater in the case of sodium than of potassium. Potassium, being retained in the filtrate, retains water with it by osmotic action resulting in diuresis. The rapid elimination of potassium is also evidenced by the rapid lowering of plasma potassium concentrations after administration of its salts or by the failure of blood concentrations to show any appreciable rise after administration of potassium salts by mouth.

This may be illustrated from an experiment of Keith and Binger.[1] Two normal subjects were placed on a fixed diet low in sodium chloride with extra fluid restricted to 800 c.c. daily for six days. Urine volume, urinary sodium, potassium and chloride, and serum potassium were determined. One subject was then given sodium chloride and one potassium chloride daily for five days in doses approximately equivalent from the molar standpoint (a total of 0.6 mols in five days). A post experimental period was also followed. A distinct difference was evident in the results of the two subjects. With sodium chloride the urine volume rose by from 100 to 200 c.c. daily but only on the last two days of the five day period. With potassium chloride the urine volume rose by slightly more than 300 c.c. daily, the rise beginning on the second day. There was a still greater difference with respect to urine chloride. On sodium chloride administration the urine chloride rose gradually throughout the five day period from a normal daily output of 20 to a maximum of approximately 180 milliequivalents. In contrast, on potassium chloride administration the chloride excretion rose from a similar control value to a prompt and sustained daily output of approximately 150 milliequivalents. As to be expected, sodium excretion paralleled chloride excretion with sodium chloride and potassium excretion paralleled chloride excretion with potassium chloride. There was also a slight increase in sodium excretion with the potassium chloride. In other words the total excretion of both water and salt was definitely greater with potassium chloride than with sodium chloride administration during the experimental period. In another series of cases in which potassium chloride was administered the urinary potassium showed concentrations up to 50 times those in the plasma. Values for plasma concentrations, on the other hand, showed little change varying from 30 to 40 mg. per cent.

As a matter of fact the slow elimination of sodium may actually promote the development of edema rather than diuresis since sodium chloride if not excreted will hold a proportionate amount of extracellular water in order to maintain isotonicity of extracellular fluids. Torbert and Cheney[2] produced puffiness of the eyelids and edema of the ankles in two normal subjects by administration of 50 mgs. of sodium chloride daily, for two days. This was associated with a decrease in plasma protein concentration, in hematocrit and in colloidal osmotic pressure of the serum the latter finding supposedly contributing to the causation of the edema. These findings are, of course, in keeping with the retention of extracellular water. It is also a common experience that in patients with edema the withholding of sodium chloride

†From the Department of Pharmacology, Tulane University of Louisiana, School of Medicine.

will result in diuresis. Stockton[3] placed two edematous patients on a salt free diet without other changes in the treatment. During the first ten days the urine volume increased 77.2 per cent above that of a previous control period on an ordinary diet. During the second ten day period the increase was 56 per cent over the volume during the control period. The blood chloride and daily chloride excretion showed little change in spite of the salt free diet. With the increased urinary volume, its chloride concentration was proportionately decreased.

In addition to the behavior of sodium and potassium salts per se they apparently play some part in the action of certain other classes of diuretics.

ACID PRODUCING SALTS SUCH AS AMMONIUM CHLORIDE AND CALCIUM CHLORIDE

These acid producing salts supply chloride to the body in excess of base since calcium is precipitated in large part in the intestine as bicarbonate and ammonia is changed to urea after absorption. This results in effect to an increase of basic ions in the body in the form of chloride and a decrease as bicarbonate producing a relative acidity. The concentration of base in the plasma remains almost stationary although it is somewhat lowered in the absence of edema due to increased excretion.

Gamble, Blackfan, and Hamilton[4] investigated the sodium and potassium exchanges under the action of acid producing salts. To illustrate this one experiment may be cited as follows: three children with edema and one without edema were placed on a fixed diet low in sodium chloride. After a control period without medication they were given calcium chloride over a three day (patients with edema) or five day (no edema) period. The average daily excretion of base for four days following the medication in excess of the excretion during a control period was as follows:

	Expressed as c.c. of 0.1 N Solution				
	Total Fixed Base	Na	K	Ca	Mg.
No edema	1242	455	569	284	37
Edema	2200	1258	751	157	54

The relatively greater increase in excretion of base in edema with no change in plasma concentration might be expected, since the edema fluid which is mobilized is a source of base. It is assumed that the potassium excretion represents elimination of intracellular water. This is in keeping with the relatively high potassium excretion in the absence of edema fluid where excess sodium and extracellular water would not be available.

This excess excretion of sodium and potassium under the action of acid producing diuretics is undoubtedly a factor in the elimination of water by virtue of their osmotic effects in the renal tubule. Of course the explanation of the freeing of the base by increased acidity is another problem.

RELATION OF SODIUM AND POTASSIUM TO THE ACTION OF MERCURIAL DIURETICS

It is generally accepted today that the important action of mercurial diuretics is by interference with renal tubular absorption[5, 6]. In the literature, however, there is much evidence that a general tissue effect plays some part in this diuretic action and some investigators have even believed this to be the main action. The general tissue effect of the mercurials involves a freeing of potassium or sodium chloride from the tissues into the plasma, and the excretion of this excess salt plays a part in the elimination of water. This may be illustrated by the work of Stockton.[3] Six edematous patients were maintained on a constant low salt diet (2 gms. of sodium chloride and 1200 c.c. of fluid) until blood and urine findings were constant for three days. Then they were given merbaphen (one dose) and the changes were as follows: Diuresis (+300 per cent) began in two hours with peaks at five and 13 hours after administration. Some diuresis continued up to 30 hours. Blood chloride increased within two hours with a peak of +6 per cent in five hours but fell below the control level in 11 hours after administration. A second peak occurred in from 18 to 21 hours (up to +4 per cent). The excretion of chloride paralleled the diuresis, the rate of excretion going as high as +2800 per cent over the control period. What is more remarkable is that the urinary concentra-

tion of sodium chloride increased in spite of the greater volume of urine, being 40 per cent above the control value during the whole period of diuresis and going as high as +75 per cent. Similar results were obtained with salyrgan on five patients but the changes involving all factors were even greater than with merbaphen.

The changes in blood chloride were slight however and Keith and Whelan[7] failed to find any constant change under the action of mercurial diuretics. If such does occur it would indicate an extrarenal action of mercurial diuretics. It is also common experience that mercurials may fail in the presence of low plasma chlorides and that the diuresis may be increased by the administration of acid producing chlorides.[7] Whether this increase could be produced by raising the blood chlorides by the administration of sodium chloride as such, without the acidity factor is doubtful. I am aware of no evidence that such is the case. Irrespective of this factor the markedly increased excretion of chloride must contribute to the increased urinary volume in the form of saline diuresis.

RELATION OF SODIUM AND POTASSIUM TO THE ACTION OF XANTHINE DIURETICS

The xanthine diuretics like the mercurials are believed to act essentially on the kidney by increasing filtration through circulatory changes or by interferences with tubular reabsorption. However here again, the diuresis is associated with sodium chloride exchanges which may well have some role in the action and which have been assigned predominant importance by some investigators. Stockton[3] also used theophylline on six edematous patients producing diuresis on the average from the 4th to 35th hour after administration. Blood chloride changes were irregular being both above and below normal during this period. The rate of chloride excretion however paralleled the diuresis, reaching a peak of 600 per cent above that of the control period and again in spite of the diuresis the chloride concentration in the urine was also above that in the control period going as high as 40 per cent above normal. Curtis[8] demonstrated that he could prevent the diuretic action of theophylline ethylenediamine in rabbits by injecting distilled water into the peritoneal cavity. The response to the diuretic was restored only after the peritoneal fluid had become isotonic. During this period of inhibition the small amounts of urine were low in chloride but when diuresis was resumed (presumably after sodium chloride had ceased going into the peritoneal fluid) the urine was high in chloride both in concentration and total amount. In these experiments also the diuresis was accompanied by raised blood chlorides. Consequently a mobilization of sodium or potassium chloride into the plasma from the tissues may be a factor in the diuretic action of the xanthines, and as with the mercurial diuretics the increased chloride excretion would tend to increase urine volume.

SUMMARY

The salts of potassium are definitely more diuretic than sodium salts. The latter, under certain conditions may actually promote the retention of edema fluid. There is evidence that an increased excretion of sodium and potassium chloride, although possibly not of major importance, is a factor in the diuretic action of the acid producing salts, the mercurials, and the xanthines.

BIBLIOGRAPHY

1. Keith, N. M., and Binger, M. W.: Diuretic action of potassium salts, J. A. M. A., 105:1584, 1935.

2. Torbert, H. C., and Cheney, G.: Reduction in colloidal osmotic pressure of blood serum after salt ingestion, J. A. M. A., 106:683, 1936.

3. Stockton, A. B.: Actions of diuretic drugs and changes in metabolism in edematous patients, Arch. Int. Med., 58:891, 1936.

4. Gamble, J. L., Blackfan, K. D., and Hamilton, B.: Study of diuretic action of acid producing salts, J. Clin. Invest., 1:359, 1925.

5. Govaerts, P.: Origine rénale ou tissulaire de la diurrèse par un composé mercuriel organique, Compt. rend. Soc. de biol., 99:647, 1928.

6. Bartram, E. A.: Experimental observations on effect of various diuretics when injected directly into one renal artery of dog, J. Clin. Invest., 11:1197, 1932.

7. Keith, N. M., and Whelan, M.: A study of the action of ammonium chloride and organic mercury compounds, J. Clin. Invest., 3:149, 1926.

8. Curtis, G. M.: Fortgesetzte Untersuchungen über die Wirkungsweise der spezifishen Diuretica. Die Blockierung der normalen Reaktion durch die intraperitoneale Injektion von destillierten Wasser, Biochem. Zeitschr., 186:95, 1927.

THE ROLE OF THE ADRENAL GLAND IN SODIUM AND WATER EXCHANGE

ALBERT SEGALOFF, M.D.†
NEW ORLEANS

Since our interest at this time is in the control of salt and water exchange, it is fitting to discuss the adrenal gland. The adrenal cortex has a profound influence upon the salt and water exchange of mammals. This is only one phase of the multiple functions of the adrenal cortex. As is well known, the adrenal glands are essential for life. They are necessary for normal protein and carbohydrate metabolism as well as for the maintenance of the general body resistance to stress.

When operative technics for adrenalectomy were perfected sufficiently so that the animals died of adrenal insufficiency several days after the operation rather than immediately from operative shock, it was noted that as adrenal insufficiency developed there was a fall in the serum sodium and chloride.[1] We are omitting such animals as the opossum and the elasmobranch fishes from our discussion since they do not show the "typical" alterations in sodium exchange which are under discussion here. Attempts at the utilization of these facts bore excellent fruit and it was found that proper therapy with sodium salts could maintain adrenalectomized animals in good condition.[2,3]

These studies were extended to patients with Addison's disease and it was found that they too could be improved by the administration of sodium salts.[4,5] The converse also was found to be true and salt restriction was applied as a diagnostic test for patients with a question of Addison's disease.[6]

The defect in the kidney appears to be an impaired ability to resorb sodium ion from the glomerular filtrate. An intriguing alternate theory has been advanced, namely, that the kidney has an impaired ability to produce ammonia. This concept is supported by the fact that when sodium excretion declines under proper therapy, the urinary ammonia content increases.

The renal wastage of sodium ion is accompanied by diuresis, which decreases as adrenal insufficiency advances and terminates with oliguria or anuria.[7] Despite the excessive urinary loss of water, the adrenalectomized animal and the patient with Addison's disease do not respond to the administration of water with diuresis. The mechanism of this loss of the diuretic response to water is not entirely clear. The adrenalectomized rat shows a delay in the time required for the stomach to empty and a deficit in intestinal absorption, but this is not the entire picture since injected water also fails to produce diuresis.[8] In addition, symptoms of water intoxication appear in the adrenalectomized animal at lower levels of water retention than in normal animals.[9]

This failure to produce diuresis is the basis for another test for adrenal hypofunction.[10] This test has a high degree of reliability and there is little apparent danger. In this procedure a measured amount of water is administered to patients suspected of having Addison's disease. If the disease is present no diuresis occurs; if not, there is a normal diuretic response to the administered water.

These urinary losses of sodium and water are reflected in a contracted circulating blood volume which is poor in sodium. Sodium ion and water then migrate from the interstitial fluid reservoirs; this creates a differential in the osmotic pressure between the body cells and their fluid environment which is naturally immediately compensated for by migration of water into the cells.[11]

As might be anticipated, these defects in sodium and water balance can be corrected by appropriate therapy with adrenal cortical extracts. Desoxycorticosterone and the amorphous fraction are particularly potent in this regard.

It has been reported that aqueous adrenal extracts can be fractionated into two frac-

†From the Alton Ochsner Medical Foundation and the Department of Medicine, Tulane University of Louisiana, School of Medicine, New Orleans, Louisiana.

tions; one is capable of maintaining life and the other affects sodium metabolism. It has further been demonstrated that it is possible to keep animals alive and in apparently excellent condition except for the low serum sodium and excessive urinary sodium loss characteristic of a severe state of adrenal insufficiency.

Of the cortical steroids, desoxycorticosterone has the most pronounced effect on salt and water metabolism. Indeed, it is so potent that it readily produces extreme sodium retention and loss of potassium and water to such a degree that muscular weakness and paralysis and even cardiac failure may occur when it is administered too vigorously.[12] When large doses of desoxycorticosterone acetate are given for a long period of time, a diabetes insipidus-like syndrome develops.[13] This is, of course, very different from diabetes insipidus since it is unaffected by pituitary antidiuretic hormone and restriction in the fluid intake does not produce dehydration. The feeding of a salt poor diet reduces the severity of the polydipsia and the polyuria. The explanation for this entire phenomenon may be that the extracellular sodium concentration is greatly increased and cellular hydration is, therefore, decreased. This is diametrically opposed to the case in adrenal insufficiency. The water intake is then greater because of an increased thirst resulting from the effects of the intracellular dehydration. In other words, the polyuria may merely be a reflection of an induced polydipsia.

The corticosterones without a hydroxyl group in the 17 position also cause sodium retention but to a lesser degree than does desoxycorticosterone. However, the introduction of a 17 hydroxyl group, as in Kendall's compound E, enhances the carbohydrate effect but reverses the effect on sodium and potassium; that is to say, the administration of compound E to an intact animal causes the renal loss of sodium and water similar to adrenalectomy and opposite to the effect of the other adrenal steroids.[14]

In the adrenalectomized animal there is also a decrease in the intestinal absorption of sodium so that there is more than just a loss of sodium ion contributing to the low serum sodium.[15]

SUMMARY

The adrenalectomized animal shows a marked loss of sodium and water in the urine which is reflected in a decreased circulating blood volume and a low serum sodium content. This, in turn, leads to a decrease in the sodium and water concentration in the interstitial fluid compartment. This is further exaggerated by the shift of water into the cells which had a higher osmotic pressure than their bathing fluids. These effects are somewhat exaggerated by an inability to absorb sodium properly from the intestinal lumen.

REFERENCES

1. Baumann, E. J., and Kurland, S.: Changes in inorganic constituents of blood in suprarenalectomized cats and rabbits, J. Biol. Chem., 71:281, 1927.

2. Rogoff, J. M., and Stewart, G. N.: Studies on adrenal insufficiency; influence of intravenous injections of Ringer's solution upon survival period in adrenalectomized dogs, Am. J. Physiol., 84:649, 1928.

3. Allers, W. D., and Kendall, E. C.: Maintenance of adrenalectomized dogs without cortin, through control of mineral constituents of diet, Am. J. Physiol., 118:87, 1937.

4. Loeb, R. F.: Chemical changes in the blood in Addison's disease, Science, 76:420, 1932.

5. Loeb, R. F.: Effect of sodium chloride in treatment of a patient with Addison's disease, Proc. Soc. Exp. Biol. & Med., 30:808, 1933.

6. Harrop, G. A., Weinstein, A., Soffer, L. J., and Trescher, J. H.: The diagnosis and treatment of Addison's disease, J. A. M. A., 100:1850, 1933.

7. Gaunt, R., Potts, H. E., and Loomis, E.: Post-adrenalectomy diuresis; effects of cortical extracts, salts and estrone, Endocrinology, 23:216, 1938.

8. Gaunt, R.: quoted by Swingle, W. W., and Remington, J. W.: Role of adrenal cortex in physiological processes, Physiol. Rev., 24:89, 1944.

9. Swingle, W. W., Parkins, W. M., Taylor, A. R., and Hays, H. W.: Study of water intoxication in intact and adrenalectomized dogs and influence of adrenal cortical hormone upon fluid and electrolyte distribution, Am. J. Physiol., 119:557, 1937.

10. Robinson, F. J., Power, M. H., and Kepler, E. J.: Two new procedures to assist in recognition and exclusion of Addison's disease; preliminary report, Proc. Staff Meet. Mayo Clin., 16:577, 1941.

11. Muntwyler, E., Mellors, R. C., Mautz, F. R., and Mangin, G. H.: Electrolyte and water equilibria in dog; electrolyte and water exchange between skeletal muscle and blood in adrenal insufficiency, J. Biol. Chem., 134:367, 1940.

12. Soffer, L. J.: Diseases of the Adrenal, Philadelphia, Lea & Febiger, 1946.

13. Ragan, C., and others: Syndrome of polydipsia and polyuria induced in normal animals by desoxycorticosterone acetate, Am. J. Physiol., 131:73, 1940.

14. Thorn, G. W., Engel, L. L., and Lewis, R. A.: Effect of 17-hydroxycorticosterone and related adrenal cortical steroids on sodium and chloride excretion, Science, 94:348, 1941.

15. Stein, L., and Wertheimer, E.: Effect of adrenalectomy on intestinal absorption involving osmotic work in rat, Proc. Soc. Exper. Biol. & Med., 46:172, 1941.

THE ANTIDIURETIC HORMONE*

THOMAS FINDLEY, M.D.†
NEW ORLEANS

All organisms which live on dry land or in hypertonic salt water possess mechanisms which enable them to conserve body water. Birds and mammals have met the problem by the development of a device which insures the reabsorption of practically all the water and much of the electrolyte content of glomerular filtrate. This device is a thin segment of tubule (Henle's loop) which lies between two convoluted portions of the kidney tubule; here, the major part of the glomerular filtrate is reabsorbed into the blood stream with the assistance of an antidiuretic hormone (ADH) secreted by the neurohypophysis. Urine volume is, therefore, regulated in large part by the action of an endocrine product upon a specific portion of the renal tubule.

Diabetes insipidus represents the loss of a biologic adaptation occasioned by failure of the neurohypophysis. Other things being equal, the rate of urine flow appears to be inversely proportional to the concentration of antidiuretic hormone circulating in the blood, and complete destruction of the neurohypophysis results in a maximal diuresis of 20 to 25 c. c. per minute for an average adult. Since the average rate of glomerular filtration is about 125 c. c. per minute,[1] it is obvious that the reabsorption of approximately 80 per cent of the glomerular filtrate is not under neurohypophyseal control. Even excessive amounts of ADH, however, will not produce complete anuria, for pitressin facilitates the reabsorption of only that water in excess of the amount required to keep the urinary solids in solution.[2] For this reason, pitressin is ineffective in controlling the polyuria in chronic nephritis, diabetes mellitus or salt diuresis.

The chemical nature of ADH is not well understood[3] and there is no general agreement as to the number of separate hormones manufactured by the neurohypophysis. It must be remembered that extracts of other organs possess antidiuretic properties—liver[4], kidney[5], and placenta.[6]

It has been clearly demonstrated that the secretion of ADH is controlled by nonmyelinated nerve fiber arising chiefly from the paired supra-optic nuclei but probably also from the paraventricular nuclei; these fibers supply the pars nervosa and with it form a functional unit. The hormone is probably manufactured by special cells in the median eminence, stalk and posterior lobe called pituicytes.[7] It has also been extracted from the supra-optic region of the dog's hypothalamus.[8] The hypothalamic nuclei are, of course, intimately connected with various parts of the central nervous system so that there are innumerable routes for impulses affecting postpituitary activity. For example, Chang and his associates[9,10] have reported that stimulation of the central end of the cut vagus results in disappearance of the secretory granules in the pituicytes and increased secretion of ADH. Boyd, Lee and Stevens[11] have claimed to produce antidiuresis by stimulating the retina of rats with flashes of light. Other examples of the reflex liberation of pituitrin have been recorded by Rydin[12] and Haterius.[13] The effects of exercise, emotion, sensory stimuli, hypnosis, conditioned reflexes and central nervous system depressants upon water excretion have been reviewed by Pickford.[14] Acetylcholine,[15] morphine[16] and nicotine[17] have been shown to exert an antidiuretic action through the mediation of the neurohypophysis and it may be that the xanthines have an opposite action. Destructive lesions of the supra-optic nuclei or of the hypothalamico-hypo-

*Read in part before the New Orleans Academy of Science, April 26, 1946.

†From the Department of Medicine, Tulane University of Louisiana, School of Medicine, and the Department of Medicine, Ochsner Clinic, New Orleans.

physeal tracts result in atrophy of the pars nervosa, in a great diminution in the amount of antidiuretic material which can be extracted from the posterior lobe, and in polyuria.[18] Destruction must be nearly complete, however, if appreciable polyuria is to result; about 85 per cent of the cells of the supra-optic nuclei must be destroyed before diuresis appears in the rat,[19] the monkey[20, 21] and the dog.[22] From experiments on dogs with diabetes insipidus showing that dehydration does not result in shrinkage of the volume of extracellular fluid, Shannon[23] concluded that the absence of ADH results in more complete tubular reabsorption of sodium as well as diminished reabsorption of water. Although it seems that maximal polyuria can be produced in experimental animals by complete destruction of the neurohypophysis even in the absence of the anterior lobe, it also seems unlikely that such complete destruction often occurs in human diabetes insipidus and that, therefore, the diuretic property of anterior lobe tissue is of clinical importance.

It may be supposed that the secretion of ADH will depend upon the need for water conservation, and a considerable amount of experimental work (for bibliography see Pickford[14]) has been done which seems to prove that dehydration results in histologic changes in the neurohypophysis, in diminution of the amount of ADH extractable from the pars nervosa, and in the appearance of ADH in the urine. There are grounds for suspecting, however, that the antidiuretic material which appears in the urine may not actually be pitressin.[6, 24, 25]

The train of events which follows the administration of large amounts of water is perhaps better understood. Rioch[26, 27] was the first to note that a small but measurable hemodilution occurs after water ingestion and that there is a time-lag of about twenty minutes between the peak of blood dilution and the peak of maximum diuresis. This phenomenon has been confirmed repeatedly and it also occurs after the intravenous administration of water.[28] It is fairly well agreed that the stimulus to water excretion consists in a relatively abrupt change in the osmotic pressure of plasma[29] but the precise mechanism whereby blood dilution increases urine formation is still open to debate. Klisiecki and associates[30] formulated what might be called the modern theory of water diuresis by postulating that hemodilution inhibits the production of ADH and that the latent period is due to the time required for the concentration of the hormone in the blood to fall below a critical level. A large body of indirect evidence is interpretable from this viewpoint, and Hart and Verney[31] have even calculated that diuresis in man will result from a fall in the plasma concentration of ADH of less than one part in fifteen billion. On the other hand, it has been shown that administration of hypertonic saline solution stimulates the production of ADH.[32, 33] Hare and co-workers[34] confirmed these findings and, by relating the concentration of chloride in the water reabsorbed by the renal tubules to the concentration of chloride in the plasma, found that pitressin does not affect chloride excretion. Chambers[35] reported that the administration of salt produced edema and a diminished hormone content of the neurohypophysis. Hickey and Hare[36] extended these observations to man and demonstrated that the intravenous injection of hypertonic saline solution increases ADH secretion. They feel that the inhibition of a pre-existing water diuresis by salt injection is good evidence that the neurohypophysis is functioning properly. As a means of distinguishing polyuria due to true diabetes insipidus from that secondary to polydipsia, they propose a test which consists in infusing 2.5 per cent sodium chloride at a standard rate during a well established diuresis. With the aid of simultaneous plasma inulin clearance determinations they calculate the concentration of chloride in the water reabsorbed by the renal tubules and compare it with the concentration of chloride in the plasma (R/P). Pituitrin (endogenous or exogenous) causes the tubules to reabsorb water in preference to chloride and diminishes the ratio to less

than 1.0; in the absence of functioning pitressin-forming tissue no antidiuresis occurs and the R/P ratio does not diminish. Shannon[37] has estimated that a dog weighing 10 to 15 kg. produces ADH at the rate of 0.001 to 0.005 units per hour.

Attractive as this theory is, the evidence is not entirely in its favor. It has been shown, for example, that urine flow may remain at low levels in decerebrate animals from which all pitressin-forming tissue has been excluded and that in these preparations the events leading up to water diuresis occurs in a perfectly normal manner.[38, 39, 40] White and Findley[41] found that a similar lag occurs in the renal excretion of chloride and glucose but not of creatinine; they felt that the latent period for all these threshold substances might be due to the time required for the renal parenchyma to become adjusted to new osmolar concentrations and that there is no need to resort to the hypopitressinemia theory. Obviously, more work is needed on this problem.

It should be stated that no clinical syndrome has been described which may reasonably be attributed to chronic hyperfunction of the neurohypophysis.

REFERENCES

1. Smith, H. W.: Lectures on the Kidney, University of Kansas, Waverly Press, 1943, Pp. 89.

2. Adolph, E. F., and Ericson, G.: Pituitrin and diuresis in man, Am. J. Physiol., 79:377, 1927.

3. Goodman, L., and Gilman, A.: The Pharmacological Basis of Therapeutics, New York, MacMillan Co., 1943.

4. Walker, A. M.: Antidiuretic effect produced by certain preparations of heparin, Proc. Soc. Exper. Biol. & Med., 39:105, 1938.

5. Pickering, G. W., and Prinzmetal, M.: Effect of renin on urine formation, J. Physiol., 98:314, 1940.

6. Ham, G. C., and Landis, E. M.: Comparison of pituitrin with antidiuretic substance found in human urine and placenta, J. Clin. Investigation, 21:455, 1942.

7. Bucy, P. C.: Pars nervosa of bovine hypophysis, J. Comp. Neurol., 50:505, 1930.

8. Melville, Eleanor, and Hare, K.: Antidiuretic material in the supra-optic nucleus, Endocrinology, 36:332, 1945.

9. Chang, H. C., Huang, J. J., Lim, R. K. S., and Wang, K. J.: Vagus-postpituitary reflex; phenomena of exhaustion and recuperation, Chinese J. Physiol., 14:1, 1939.

10. Chang, H. C., Chia, K. F., Huang, J. J., and Lim, R. K. S.: Vagus-postpituitary reflex; antidiuretic effect, Chinese J. Physiol., 14:161, 1939.

11. Boyd, E. M., Lee, B. K., and Stevens, M. E. T.: Effect of optical stimuli on output of urine in albino rats, Endocrinology, 32:27, 1943.

12. Rydin, H., and Verney, E. B.: Inhibition of water diuresis by emotional stress and by muscular exercise, Quart. J. Exper. Physiol., 27:343, 1938.

13. Haterius, H. O.: Evidence of pituitary involvement in experimental control of water diuresis, Am. J. Physiol., 128:506, 1940.

14. Pickford, Mary: Control of the secretion of antidiuretic hormone from the pars nervosa of the pituitary gland, Physiol. Rev., 25:573, 1945.

15. Pickford, Mary: Inhibitory effect of acetylcholine on water diuresis in dog, and its pituitary transmission, J. Physiol., 95:226, 1939.

16. De Bodo, R. C.: The antidiuretic action of morphine, and its mechanism, J. Pharm. & Exper. Therap., 82:74, 1944.

17. Burn, J. H., Truelove, L. H., and Burn, Isabel: The antidiuretic action of nicotine and of smoking, Brit. M. J., 1:403, 1945.

18. Fisher, C., Ingram, W. R., and Ranson, S. W.: Diabetes Insipidus and the Neuro-Hormonal Control of Water Balance, Ann Arbor, Edwards Bros., 1938.

19. Richter, C. P.: Pituitary gland in relation to water exchange. A. Research Nerv. & Ment. Dis., (1938) Proc., 17:392, 1938.

20. Magoun, H. W., Fisher, C., and Ranson, S. W.: Neuro-hypophysis and water exchange in monkey, Endocrinology, 25:161, 1939.

21. Rasmussen, A. T., and Gardner, W. J.: Effects of hypophysial stalk resection on hypophysis and hypothalamus of man, Endocrinology, 27:219, 1940.

22. Heinbecker, P., and White, H. L.: Hypothalamico-hypophysial system and its relation to water balance in the dog, Am. J. Physiol., 133:582, 1941.

23. Shannon, J. A.: Control of renal excretion of water; effect of variations in state of hydration on water excretion in dogs with diabetes insipidus, J. Exper. Med., 76:371, 1942.

24. Walker, A. M.: Experiments upon relation between pituitary gland and water diuresis, Am. J. Physiol., 127:519, 1939.

25. Gersh, I.: Water metabolism: endocrine factors, A. Research Nerv. & Ment. Dis., Proc. (1939), 20:436, 1940.

26. Rioch, D. M.: Experiments on water and salt diuresis, Arch. Int. Med., 40:743, 1927.

27. Rioch, D. M.: Water diuresis, J. Physiol., 70:45, 1930.

28. Newton, W. H., and Smirk, F. H.: The effect of the intravenous administration of water upon the rate of urine formation, J. Physiol., 78:451, 1933.

29. Chambers, G. H., Melville, Eleanor, Hare, Ruth and Hare, K.: Regulation of the release of pituitrin by changes in the osmotic pressure of the plasma, Am. J. Physiol., 144:311, 1945.

30. Klisiecki, A., Pickford, Mary, Rothschild, P., and Verney, E. B.: The absorption and excretion of water by the mammal. II. Factors influencing the response of the kidney to water ingestion, Proc. Roy. Soc. Series B, 112:521, 1933.

31. Hart, P. D'A., and Verney, E. B.: Observations on the rate of water-loss by man at rest; description of constant temperature and humidity room; "spontaneous" diuresis during prolonged rest, Clin. Sc., 1:367, 1934.

32. Gilman, A., and Goodman, L.: Secretory response of posterior pituitary to need for conservation, J. Physiol., 90:113, 1937.

33. Ingram, W. R., Ladd, L., and Benbow, J. T.: Excretion of antidiuretic substance and its relation to hypothalamico-hypophyseal system in cats, Am. J. Physiol., 127:544, 1939.

34. Hare, R. S., Hare, K., and Phillips, D. M.: Renal excretion of chloride by normal and by diabetes insipidus dog, Am. J. Physiol., 140:334, 1943.

35. Chambers, G. H.: Histological and hormonal changes in the neurohypophysis of rats following NaCl administration, Fed. Proc., 4:13, 1945.

36. Hickey, R. C., and Hare, K.: Renal excretion of chloride and water in diabetes insipidus, J. Clin. Invest., 23:768, 1944.

37. Shannon, J. A.: Control of renal excretion of water; rate of liberation of posterior pituitary anti-

diuretic hormone in dog, J. Exper. Med., 76:387, 1942.
38. Fee, A. R.: Studies on water diuresis; effect of decerebration anesthesia and morphia upon water diuresis, J. Physiol., 68:39, 1929.
39. Fee, A. R.: Studies on water diuresis; excretion of urine after hypophysectomy and decerebration, J. Physiol., 68:305, 1929.
40. Newton, W. H., and Smirk, F. H.: The pituitary gland in relation to polyuria and to water diuresis, J. Physiol., 81:172, 1934.
41. White, H. L., and Findley, T.: Time relations in renal excretion of threshold and no-threshold substances, Am. J. Physiol., 119:740, 1937.

THE DIURETIC HORMONE

WILLIAM PARSON, M.D.†
NEW ORLEANS

The title of this paper is provocative rather than descriptive. Is there a diuretic hormone? Is there a hormone which is the antagonist of the antidiuretic hormone of the neurohypophysis? Are there possibly a number of diuretic hormones? Or, perhaps, the term is a misnomer and it would be better to speak of the "diuretic forces" to represent the non-specific effect of the various catabolic agents producing waste products which tend to augment urine flow.

This paper represents no new material. Certain concepts will be reviewed and evaluated.

The disturbed physiology of diabetes insipidus has been discussed in a previous paper in this symposium. It was to be expected that a diuretic hormone would be sought for as an explanation for the profound diuresis seen in diabetes insipidus. It became apparent, however, that the diuresis of diabetes insipidus was caused by a deficiency of the antidiuretic hormone of the neurohypophysis.

In 1918 von Hann[1] pointed out that in man the pars anterior of the hypophysis must be at least partially intact if destruction of the neurohypophysis is to result in diabetes insipidus. It is of interest to examine the evidence for this concept. Von Hann reviewed the necropsy findings in 20 cases of diabetes insipidus. The pars anterior was either wholly or partially intact while the neurohypophysis was "destroyed" in 17 of these cases. In the three remaining cases the state of the pars anterior was not noted. This group of cases was contrasted with nine cases of Simmond's disease in which there was said to be a total destruction of the hypophysis; diabetes insipidus was not encountered in any of these cases.

The concept of von Hann has had wide clinical support through the years. Diabetes insipidus and Simmond's disease have appeared to be mutually exclusive. Any number of clinical cases[2] have been described in which diabetes insipidus was succeeded by Simmond's disease with amelioration of the diabetes insipidus. At necropsy total destruction of the hypophysis is described. It has been assumed that the clinical sequence was caused by a progressive lesion involving the hypophysis which destroyed first the neurohypophysis producing diabetes insipidus and then spread to the pars anterior causing Simmond's disease and "curing" the diabetes insipidus.

There has recently been reported a case of severe permanent diabetes insipidus occurring in what was said to be pituitary dwarfism.[3] At necropsy bilateral localized lesions in the hypothalamus with complete destruction of the neurohypophysis were described. The hypothalamic lesions were limited almost entirely to the region of the supraoptic nuclei. There was almost complete disappearance of the cells of the paraventricular nuclei. Careful histologic study of the pars anterior revealed fibrosis; the total number of cells was estimated at about one-sixth of normal.

It would appear then that if the von Hann concept is correct, a relatively small fraction of the pars anterior may suffice for the production of diabetes insipidus provided there is adequate destruction of the neurohypophysis.

Experimental support for the von Hann concept was slow to appear. In 1934 Richter[4] described his work in rats. He produced diabetes insipidus by lesions of the supra-optico-hypophyseal system. He was unable to produce permanent diabetes in-

†From the Department of Medicine, Tulane University of Louisiana, School of Medicine, and the Department of Medicine, Ochsner Clinic, New Orleans.

sipidus unless some functioning pars anterior remained intact in the animals. These experiments were confirmed by others[5]. However, in 1941, Heinbecker and White[6] were able to produce permanent diabetes insipidus in nine dogs by total destruction of the neurohypophysis and concomitant removal of the entire pars anterior. They confirmed the fact that there was no pars anterior intact at all by careful histologic studies. They made meticulous studies of the number of intact cells in the supra-optic nuclei in their experimental animals and they concluded that the survival of less than 3 per cent of intact cells in the supra-optic nuclei was the key feature in the production of permanent diabetes insipidus in dogs.

These rather conclusive experiments bring up a number of important points. Heinbecker and White are very critical of previous work because of inadequate histologic evaluation of both experimental and clinical lesions. Their criticisms are just. However, without further studies it is not justifiable to carry over the results in the dogs to the rats and man. Our comments will then be limited to the dog; it should be noted that the experiments of Heinbecker and White do not rule out a possible diuretic hormone produced by the pars anterior nor do they eliminate the possibility that the pars anterior may act as a diuretic force. The fact is that the pars anterior is not essential for total diabetes insipidus in the dog if there is "total" destruction of the neurohypophysis.

Let us approach the problem from a somewhat different angle. If the pars anterior has a diuretic activity, it might be expected that extracts prepared from it would produce polyuria when administered to animals. There is adequate evidence to show that this does occur. Cushing and his coworkers[7] in 1910 augmented considerably the urine flow by the administration of a pars anterior extract to a dog with mild experimental diabetes insipidus. Numerous experiments[8] have been performed in which normal and mildly polyuric animals, including dogs, cats and rabbits were used; most of the experiments[9] have confirmed the presence of a diuretic effect from the administration of these extracts. However, there have been a number of negative results, chief among which are those of White[9] who has been unable to produce diuresis in normal rats with pars anterior extracts.

These experiments are difficult to evaluate. Extracts of the pars anterior which were mixtures of hormone fractions and various protein breakdown products have been used. Diuretic effects have been described by experimenters[8] who used acid extracts, alkaline extracts, salt suspensions, predominently growth factor, predominently thyrotropic factor and others. Precise experiments must wait until "pure" pituitary fractions are available for experimentation.

If we accept this body of evidence that there is a diuretic effect produced by the administration of pars anterior extracts, can we delineate any further the mode of action? It is reasonable that an action on water excretion might be the resultant of the many life processes controlled and maintained by the pars anterior of the pituitary. The changes that occur following ablation of the pars anterior are characterized by the loss of the various trophic functions with secondary atrophy of the thyriod, the adrenal, the gonads, and other organs. It is clear that the decreased metabolic exchange under these circumstances will be manifested by a small urine output and it is to be expected that replacement therapy with extract of the pars anterior will result in a return to a higher level of activity of the endocrine glands and a commensurate rise in urine output.

The search for a diuretic hormone is more specific than this. Is there evidence of a diuretic effect which can be explained by direct hormonal effect on the kidney function itself by an extract of the pars anterior? Or, is there possibly a direct effect by the thyroid or adrenals so that the pars anterior is indirectly involved through its trophic functions?

Several workers[10, 11] have recently emphasized the marked influence of the hy-

pophysis on the kidney by demonstrating that the expected hypertrophy of the remaining kidney following unilateral nephrectomy does not occur in the hypophysectomized animal.

More recently, a number of careful and extremely important studies[12] have been made of the effects of extracts of the pars anterior or some specific renal functions. These studies were a logical follow up of some previous studies[13] on the effect of hypophysectomy on these same renal functions.

These experiments were performed on several types of animals which had been operated on. For our purposes the discussion will be limited to the dogs with ablation of the pars anterior. The clearance technics were used. Inulin clearance (glomerular filtration), diodrast clearance (effective renal blood flow) and diodrast-Tm (tubular mass) were determined. It was observed that the renal blood flow fell in five days to 50 to 60 per cent of the control level; the glomerular filtration paralleled this fall; the diodrast-Tm in the same space of time fell to 25 to 30 per cent of the control level. These effects were noted to last at least a year. A number of observations were made which indicated that these striking changes were not due to a fall in blood volume nor a fall in the blood pressure. It was reasoned further that these changes were not due to decreased metabolic rate since hypophysectomized dogs will take six to eight weeks to have a fall of 20 per cent in the metabolic rate. The effects above were apparent in less than a week and were of greater degree.

Studies were then made to determine whether administration of an extract of the pars anterior would be effective in returning these renal functions to normal in animals in which the pars anterior had been ablated, and also to determine whether normal dogs would have augmentation of these renal functions. The results were very striking; the increase of the effective renal blood flow (diodrast clearance), filtration rate (inulin clearance) and tubular mass (diodrast-Tm) was obtained in the normal dog; even more effect was noted in the animals in which there had been a depression due to removal of the pars anterior.

Unfortunately, no measurements were made of urine flow in these experiments. However, it is not unreasonable to assume that the urine flow paralleled the renal blood flow in these animals. These observations need verification, of course, and particular attention should be paid to the urine flow.

More precise studies will have to be made of cardiac output and the blood flow through organs other than the kidney in order to establish the specificity of the reported renal changes.

Is this reputed action of the pars anterior on kidney function mediated through one or several of the trophic hormones or is it a direct action of a "new" hypophyseal fraction? The answer is not available but there are a number of interesting facts which bear upon the question. The possibility that the described effect of the pars anterior is mediated through the thyroid has been given serious consideration. As described early in this paper, diuresis was produced in several types of animals by the administration of pars enterior extracts. It was discovered that these extracts did not produce diuresis in the absence of the thyroid gland[14]. It may be that the thyrotropic factor contributes to the diuretic effect but these studies of White and Heinbecker[15] demonstrate that the diuretic principle is not solely the thyrotropic hormone. It was shown that with a constant intake of thyroid insufficient in itself to produce diuresis, the thyroidectomized dog showed a diuretic response to pars anterior administration which was ineffective without thyroid. They suggested that in the dog thyroid might provide some sensitizing of the organism to the diuretic principle of the pars anterior or possibly thyroid might set the proper stage for pars anterior diuretic action by increasing the metabolic rate.

It would be most interesting to see the experiments of Heinbecker and White concerned with the changes in renal function (inulin clearance, diodrast clearance) per-

formed in thyroidectomized and hypophysectomized-thyroidectomized dogs. It would be of great interest to know if the administration of pars anterior extract would produce any augmentation of the renal flood flow, etc. in the absence of the thyroid gland. These authors[12] have shown that thyroid administered to normal dogs and hypophysectomized dogs will result in augmentation of the renal blood flow and filtration rate similar to but not quite so large as occurs with pars anterior extracts.

In addition to the evidence presented in the preceding paragraphs, it is clear that the diuretic function of the pars anterior is not mediated solely through the thyroid gland via the thyrotropic hormone since total thyroidectomy does not cure diabetes insipidus. Findley and Heinbecker[16] reported that total thyroidectomy in a patient with diabetes insipidus diminshed the diuretic effect of sodium chloride and increased the antidiuretic effect of pitressin. It failed, however, to reduce urine flow below the limits set by a low salt diet.

Not too much needs to be said concerning the role of the adrenal as a diuretic force since one of the papers (Segaloff, A.: The Role of the Adrenal Gland in Sodium and Water Exchange) of this symposium is devoted entirely to the role of the adrenal in electrolyte control. There are several features of adrenal physiology which pertain especially to the problem on hand and should be mentioned.

Adrenal cortical extracts were studied for their effects on renal function (inulin clearance, diodrast clearance) parallel to the studies already mentioned[12] in which pars anterior extract and thyroid were used. It was found that inulin and diodrast clearances were unaffected or somewhat decreased by the administration of adrenal cortical extract to normal dogs and dogs with lesions in the hypophysis. The diodrast and inulin clearances, however, were increased in dogs in whom bilateral hypothalamic lesions had been produced. Diodrast-Tm was decreased in all the experimental dogs studied. These studies would tend to show at least that the effect of the pars anterior extract was not mediated through the cortical trophic hormone. The significance of the unique effect of the adrenal cortical extract in the hypothalamic puncture dogs is not sufficiently clear to discuss at the present time.

Studies of water diuresis have brought to light certain facts with reference to the adrenal cortex. There is evidence that the lack of normal water diuresis in hypophysectomized rats is due to the atrophic adrenals[17]. Water diuresis will not occur in hypophysectomized rats which are treated with pars anterior extracts (which will restore appetite growth) or thyroid (which will restore normal basal metabolic rate) or a combination of both. However, water diuresis is almost completely restored by relatively small amounts of adrenal cortical extract or desoxycorticosterone acetate. It is not clear whether this effect is mediated through a direct effect on the kidney or whether it represents the result of an effect on the shift of water between the cells and the extracellular spaces. Or conceivably, the adrenal may influence the release of the antidiuretic hormones, or, the sensitivity of the kidney to this hormone. Along the same line, and as poorly understood, should be mentioned the diabetes insipidus-like picture produced in dogs by the administration of very large doses of desoxycorticosterone acetate.[18] Finally, it should be mentioned that certain adrenal cortical fractions such as compound E in addition to an effect on carbohydrate metabolism tend to favor the excretion of salt and water[19].

The "diuretic role" of the adrenal requires considerable elucidation before it can be properly evaluated.

Is there a diuretic hormone? This paper has not produced the answer. If it has done anything, it has justified the asking.

REFERENCES

1. Von Hann, F.: Ueber die Bedeutung der Hypophysenveranderungen bei Diabetes Insipidus, Frankf. Ztschr. f. path., 21:337, 1918.

2. Fisher, C., Ingram, W. R., and Ranson, S. W.: Diabetes Insipidus and the Neurohormonal Control of Water Balance, Edwards Bros., 1938, Pp. 155.

3. Baker, A. B., and Craft, C. B.: Bilateral localized lesions in hypothalamus with complete destruction of

neuro-hypophysis in pituitary dwarf with severe permanent diabetes insipidus, Endocrinology, 26:801, 1940.

4. Richter, C. P.: Experimental diabetes insipidus: its relation to the anterior and posterior lobes of the hypophysis, Am. J. Physiol., 110:439, 1934.

5. Pencharz, R. I., Hopper, J. Jr., and Rynearson, E. H.: Water metabolism of rat following removal of anterior lobe of hypophysis, Proc. Soc. Exper. Biol. & Med., 34:14, 1936.

6. Heinbecker, P., and White, H. L.: Hypothalamico-hypophysial system and its relation to water balance in dog, Am. J. Physiol., 133:582, 1941.

7. Cushing, H., and Goetsch, E.: Concerning the secretion of the infundibular lobe of the pituitary body and its presence in the cerebrospinal fluid, Am. J. Physiol., 27:60, 1910.

8. Fisher, C., Ingram, W. R., and Ranson, S. W.: Diabetes Insipidus and the Neurohormonal Control of Water Balance, Edwards Bros., 1938, Pp. 157-158.

9. White, H. L.: Pituitary gland influences on water balance in rat, Am. J. Physiol., 119:5, 1937.

10. Winternitz, M. C., and Waters, L. L.: Effect of hypophysectomy on compensatory renal hypertrophy in dogs, Yale J. Biol. & Med., 12:705, 1940.

11. White, H. L., Heinbecker, P., and Rolf, D.: Effects of hypophysectomy on some renal functions, Proc. Soc. Exper. Biol. & Med., 46:44, 1941.

12. Heinbecker, P., Rolf, D., and White, H. L.: Effects of extracts of hypophysis, thyroid and adrenal cortex on some renal functions, Am. J. Physiol., 139:543, 1943.

13. White, H. L., Heinbecker, P., and Rolf, D.: Effects of removal of anterior lobe of hypophysis on some renal functions, Am. J. Physiol., 136:584, 1942.

14. Barnes, B. O., Regan, J. F., and Bueno, J. G.: 'Is there a specific diuretic hormone in the anterior pituitary? Am. J. Physiol., 105:559, 1933.

15. White, H. L., and Heinbecker, P.: Pituitary regulation of water exchange in dog and monkey, Am. J. Physiol., 118:276, 1937.

16. Findley, T., and Heinbecker, P.: Total thyroidectomy for human diabetes insipidus, Proc. Soc. Exper. Biol. & Med., 36:448, 1937.

17. Joseph, S., Schweizer, M., Ulmer, N. Z., and Gaunt, R.: Anterior pituitary and its relation to adrenal cortex in water diuresis, Endocrinology, 35:338, 1944.

18. Ragan, C., Ferrebee, J. W., Phyfe, P., Atchley, D. W., and Loeb, R. F.: Syndrome of polydipsia and polyuria induced in normal animals by desoxycorticosterone acetate, Am. J. Physiol., 131:73, 1940.

19. Thorn, G. W., Engel, L. L., and Lewis, R. A.: Effect of 17-hydroxycorticosterone and related adrenal cortical steroids on sodium and chloride excretion, Science, 94:348, 1941.

TURNOVER OF WATER AND SALT*

PAUL B. REASER, M.D.†
AND
GEORGE E. BURCH, M.D.†
NEW ORLEANS

Sodium and water are two of the most difficult of biologic substances to analyze and evaluate quantitatively. Because of this very little is known about their behavior in the human body. The introduction of tracer elements (Na^{24}, Deuterium) has partially increased our understanding but there is still much to be learned. This discussion is not an attempt to review the existing data, but is merely a summary of that which is of interest to the physician.

WATER

A 70 kilogram adult contains approximately a 50 liters of water divided into three compartments: the intracellular, containing about 35 liters; the interstitial, containing about 11 liters; and the vascular, containing about four liters.[1] Water taken in the gastrointestinal tract distributes itself throughout these compartments very readily and within an hour is in equilibrium with 60 per cent of the body weight.[2] Such water has an average stay in the body of approximately 14 days.[2] Normally it is taken in only through the gastrointestinal tract and lost from urinary, intestinal and respiratory tracts and through the skin. Of these routes of excretion, sweating is the most variable while diffusion through the skin is one of the most constant.

The rate of physical turnover in the body cannot be accurately measured but the information thus far available throws a great deal of light on such problems as edema formation. Nothing is known quantitatively of the exchange between the intra-cellular and interstitial compartments except the results of the studies of Darrow[3] These studies are concerned with fluid shifts resulting from electrolyte disturbance so are not applicable to this particular discussion (see below). The exchange between the vascular and interstitial compartments has been investigated by Flexner et al.[4] who find that 73 per cent of the blood water exchanges with extravascular fluid every minute. This is about three liters per minute or 4000 liters per day. From this exchange there is a surplus amounting to the lymph formed. This has been estimated as 40-50 liters per day or 99 per cent returned with 1 per cent as lymph. This same relationship is approximated by the kidneys in that 180 liters of water are passed into the glomerular filtrate with 1500-1800 c.c. ex-

*Aided by a grant from the Helis Institute for Medical Research, Mrs. E. J. Caire Research Fund and the Rockefeller Foundation.

†From the Department of Medicine, Tulane University of Louisiana, School of Medicine, and Charity Hospital, New Orleans, La.

creted as urine. Approximately 10 liters are exchanged in the gastrointestinal secretions per day.

When water is considered as a chemical compound we find an additional exchange taking place which is of the same magnitude as the physical turnover. Barbour[2] states that one-third of the hydrogen atoms of protein and carbohydrates are in exchange with hydrogen atoms of water. What this means in terms of body water is not as yet apparent but the identity of water as a simple solvent must be reconsidered.

SODIUM

There are approximately 50 grams of sodium in a 70 kilogram adult. This is divided between two compartments instead of three as is the case with water, 34 grams in interstitial compartment and 15 grams in plasma. Little if any is contained within cells. Normally from 3-10 grams are taken in each day. An equal amount is excreted. The average life of sodium in the human body is not known with any certainty because the tagged molecules (Na^{24}) have an average life of only 21.2 hours. A longer life isotope is expected to yield information on this point. When taken in the gastrointestinal tract it appears quickly in the blood and urine. It is distributed only in the extracellular fluid of the body (20-25 per cent of body weight.[3]) In man it exists in concentrations of approximately 145 milliequivalents per liter in blood and interstitial fluid. When this value is exceeded it can mean one of two things: (1) Actual increase in sodium of body with corresponding increase in water; or (2) same amount of sodium but reduced amount of water for solution. The converse is true for lower values. These relationships must be kept in mind in evaluating blood sodium levels.

Sodium is not exchanged between the intracellular and interstitial compartments to any measurable extent. Gellhorn et al.[6] state that 56 per cent of plasma sodium diffuses through capillaries per minute. This is equivalent to 11 kilograms per day. The transfer in the kidney differs because sodium is retained but if calculated on the basis of glomerular filtrate concentration and reabsorption per cent (99.6)[1] it can be seen that approximately 900 grams are filtered through and 896 grams reabsorbed per day. Sodium is secreted into the gastrointestinal tract in concentrated form and by the sweat glands in a dilute form compared to plasma levels. In view of these figures it can be seen that imperceptible changes from the normal can produce marked changes in internal environment.

Considered chemically sodium is a very active ion and is exchanging constantly with similar ions in other sodium containing molecules ($NaHCO_3$, NaH_2PO_4, Na_2HPO_4). In addition there is another exchange not usually considered. Hodge et al.[7] have shown that approximately 21 per cent of the body sodium is combined with bone calcium (adsorbed to the hydroxyapatite crystal). This combination is one that readily takes up sodium from the fluid surrounding it when the molecular ratio with calcium is less than 1-30 and will release it slowly when this fluid becomes depleted. Such a mechanism provides a valuable reservoir in the body. The magnitude of 21 per cent of total sodium must modify current concepts of sodium balance.

Perhaps Na^{22} with its long average life of four and a fourth years will help to solve some of the problems of importance in sodium balance in health and disease.

In conclusion a brief outline of the effect of sodium depletion and excess will be given.

1. Marked deficiency of sodium (McCollum low sodium diet 00.2 per cent Na). Results: There is increased excretion of sodium when the intake is increased. This is similar to adrenalectomized animals and is prevented by cortical extract.

2. Moderate to borderline deficiency results in a retention of sodium greater than normal.[5]

3. A marked increase in sodium intake (20 gm./day for three days), results in excretion of a part of the sodium and an increase in the extracellular fluid compartment with normal re-established in three

days. When it is stopped diuresis starts in 12 hours and in 24 hours equilibrium is back to normal in regards to sodium and water (Darrow[3]).

4. An increase in sodium excretion caused with NH_4Cl being given for three days results in salt and H_2O both being lost with a decrease in the extracellular compartment. Normalcy is established in three days (Darrow[3]).

5. Adrenalectomized rats show an increased total sodium excretion including sodium added to diet; reverse is true of potassium. If sodium is available in moderate quantities (1 per cent in drinking water), sodium and potassium excretion becomes normal.[9]

CONCLUSION

As is true with any investigation of fundamental processes the addition of information such as this serves primarily to raise more questions and reveal more acutely a need for more information.

REFERENCES

1. Gamble, J. L.: Lecture Syllabus, Harvard Medical School, 1942.

2. Barbour, H. G.: Basis of pharmacological action of heavy water in mammals, Yale J. Biol. & Med., 9:551, 1937.

3. Darrow, D. C.: Body-fluid physiology: the relation of tissue composition to problems of water and electrolyte balance, New England J. M., 223:91, 1945.

4. Flexner, L. B., Gellhorn, A., and Merrell, M.: Studies on rates of exchange of substances between blood and extravascular fluid; exchange of water in guinea pig, J. Biol. Chem., 144:35, 1942.

5. Kaltreider, N. L., Mencely, G. R., Allen, J. R., and Bale, W. F.: Determination of volume of extracellular fluid of body with radio-active sodium, J. Exper. Med., 74:569, 1941.

6. Gellhorn, A., Merrell, M., and Rankin, R. M.: Rate of transcapillary exchange of sodium in normal and shocked dogs, Am. J. Physiol., 142:407, 1944.

7. Hodge, H. C., et al: Nature of insoluble sodium of bone. Adsorption of sodium at 40 degrees by bone, dentin, enamel and hydroxyapatite as shown by radioactive isotope, J. Biol. Chem., 148:321, 1943.

8. Anderson, E., and Joseph, M.: Electrolyte excretion studies in rats maintained on low Na and low K diets, Proc. Soc. Exper. Biol. & Med., 40:344, 1939.

9. Anderson, E. and Joseph ,M.: Urinary excretion of radioactive Na and K in adrenalectomized rats, with and without salt, Proc. Soc. Exper. Biol. & Med., 40:347, 1939.

WATER AND SODIUM BALANCE IN CONGESTIVE HEART FAILURE*

GEORGE BURCH, M.D.†
AND
PAUL REASER, M.D.†
NEW ORLEANS

That the mechanism of congestive heart failure is not fully established is generally agreed. Many clinicians, nevertheless, accept the ideas of "forward" and "backward" failure with a sense of satisfaction and complacency and fail to make any serious attempts to question them. There are many data which cast strong doubt on them. Unfortunately these data, though sufficient to question the validity of the classical concepts, are insufficient to establish a satisfactory explanation for congestive heart failure. Since congestive heart failure is so common and the problems of edema so important, it is the purpose of this presentation to summarize briefly some of the data found difficult to explain on the two generally accepted theories of congestive heart failure and to present a different concept.

Before entering into a discussion the two classical concepts of the mechanism of congestive heart failure are summarized.[1] The earlier of the two, "Forward Failure Theory," is based upon the idea that cardiac output is decreased and is, therefore, often referred to as the "Decreased Cardiac Output Theory." According to this theory the decrease in cardiac output results in anoxia in the tissues. This is followed by an increase in capillary permeability and edema with the classical clinical picture. This theory requires therefore that:

1. The cardiac output must be decreased for the period of the congestive heart failure syndrome.

2. The cardiac output must increase before improvement occurs, and

3. States which decrease the cardiac out-

*Aided by a grant from the Helis Institute for Medical Research, Mrs. E. J. Caire Research Fund and the Rockefeller Foundation.

†From the Department of Medicine, Tulane University of Louisiana, School of Medicine, and Charity Hospital, New Orleans, La.

put must increase the severity of the congestive heart failure.

In the "Backward Failure Theory," it is stated that overwork of the heart leads to dilatation of the ventricle with the accumulation of blood because of a decrease in cardiac output (probably for only a few beats), an accumulation of blood in the veins with a resultant increase in venous pressure and venous blood volume. This is followed by an increase in intracapillary, hydrostatic pressure, circulatory stasis, capillary endothelial anoxia and an increase in capillary permeability with the resultant edema and classical picture of congestive heart failure. This theory would necessitate at least:

1. A decrease in cardiac output at some time,

2. High protein concentration in the edema fliud, and

3. Increase in venous pressure before the onset of congestive heart failure.

There are many observers who believe that both theories are required to explain the clinical picture of congestive heart failure.

In cardiac edema, there is an increase in volume of all of the fluid compartments, that is, (1) volume of the blood, (2) volume of the intercellular fluid, and (3) volume of the intracellular fluid. The intercellular fluid is isotonic, at a pH of 7.4, essentially normal in electrolyte concentration and relatively low in protein concentration (0.5 gram per 100 c.c.)

FACTS DIFFICULT TO EXPLAIN

There are many bits of data which make one question seriously the entire validity of the two classical concepts. Many of these are well known to every clinician, but in many instances these have never been considered collectively as serious objections to the two theories. These are:

1. Ligation of a large vein, the inferior vena cava just below the renal veins, will result in venous pressure values of 600 or more m.m. of water pressure in the tributaries without the development of clinical edema in the areas drained. It may be said that this is seriously different from the venous hypertension of congestive heart failure in that the renal circulation and renal function are not disturbed. This objection is over-ruled by the fact that in concretio cordis or mediastinal vena cava obstruction there is often marked venous hypertension for prolonged periods without clinical edema. In these states the renal circulation is distributed.

2. The intracapillary pressure in the capillaries of the feet increases to high levels when an individual stands erect. This pressure is often greater than the intra-arterial pressure in the arteries of the arms. Still clinical evidence of edema is not present. The tall man is no more prone to develop edema of the feet on standing than a short person. Therefore, the role of hydrostatic pressure in cardiac edema is very difficult to evaluate and is certainly not of the great value it is claimed to be.

3. There is no clinical edema in many severe anoxic states such as in tetralogy of Fallot or at high altitudes. With this anoxia, more severe than in congestive heart failure, there is no evidence of increase in capillary permeability, with edema formation. Such findings as these make it difficult to understand the importance of anoxia as a factor producing edema in congestive heart failure.

4. Patients with heart disease often gain weight before there is any increase in venous pressure. This again reduces the importance of increase in venous pressure or hydrostatic pressure in the explanation of cardiac edema.

5. Patients with heart disease who gradually and progressively go into congestive heart failure have been shown to present a drop in cardiac output without any rise in venous pressure when in Functional Class II. This is difficult to explain by either the "Forward" or "Backward" theories. Furthermore, when the failure progresses to the Functional Class III phase there was observed a simultaneous increase in both the cardiac output and venous pressure, findings which would be expected in view of Starling's law of the heart.[2] The re-

lationship of increase in venous pressure to cardiac output fails to abide by expectations planned by the two classical theories. Incidentally, the cardiac output has been found to be either decreased, increased or unchanged in patients with congestive heart failure.

6. The low protein content of the cardiac edema fluid, 0.5 gram per 100 c.c. is also difficult to explain by either of the two theories. If there was an increase in capillary permeability from anoxia there would necessarily be an increase in the concentration of protein in the edema fluid. The low protein content reduces the importance of capillary wall anoxia and increase in capillary permeability as a factor in the edema formation.

7. Extensive burning of the right ventricle of the dog with almost complete destruction of the entire myocardial tissue (checked by histologic sections) failed to be followed by a pattern of congestive heart failure.[3] Ligation of the coronary arteries to the right ventricle of the dog also failed to produce congestive heart failure. These observations are rather difficult to interpret in the light of the two classical theories.

8. The plasma proteins are usually normal, but may be elevated and are not usually low. Therefore, the edema and picture of congestive heart failure cannot be explained by changes in colloid osmotic pressure.

9. There is a decrease in cardiac output with venesection followed by clinical improvement. This is difficult to accept on the basis of the "forward" failure theory. With a decrease in cardiac output there should follow an increase in the severity of the failure.

10. A low salt diet is often followed by an improvement of the patient in congestive failure. Such a diet has no direct effect on the heart. This is difficult to explain satisfactorily by the two classical theories.

11. An over-does of desoxycorticosterone results in a clinical picture which is similar to that of congestive heart failure. This picture develops without there being any known direct cardiac change responsible for the syndrome.[4]

FINDINGS WHICH SUPPORT ANOTHER NEGLECTED MECHANISM

For many years there have been a gradual accumulation of data supporting a renal mechanism for most if not all of the syndrome of congestive heart failure. The idea that the kidneys may play an important role in congestive heart failure is not a new one. Baynard as early as 1722 suggested the idea.[5] Furthermore, it has been well known for many years that congestive heart failure is associated with an abnormal urine. There may be hematuria, albuminuria, many casts, a decrease in phenolsulfonphthalein excretion, and azotemia. These changes may reach high levels of abnormalities at times. They are usually casually referred to as being result of the "congestion of the kidneys." Little attention has been given to these changes as possible renal expressions suggesting a renal mechanism for the heart failure.

Before entering into a discussion of some of the newer data supporting a renal factor in heart failure it is well to point out three definite facts. There may be a possible exception to the first.

They are:

1. The initiating factor in the clinical syndrome of congestive heart failure is in the heart.

2. When a patient first sees his physician all of the accumulated fluid and electrolyte entered through the gastrointestinal tract. and

3. The renal excretion of salt and water lagged behind the intake, that is, at some time the patient was in a positive balance.

Therefore, by virtue of fact three above, regardless of the mechanism the kidneys have certainly failed to excrete enough salt and water.

DATA IN SUPPORT OF A RENAL MECHANISM FOR CONGESTIVE HEART FAILURE

There are certain observations which indicate a renal role in the congestive heart failure syndrome. These data are not complete and are so inadequate that no conclusions can be reached at present. They are

sufficient, however, to support a need for careful study of the relationship of renal function to heart failure. The findings are:

1. The well known marked diuresis and improvement of a patient with congestive heart failure treated with mercurial diuretics show how effective a change in renal function can influence the heart failure syndrome. There is no known direct effect of the diuretic on the heart, the improvement being initiated elsewhere. The general impression is that the action is mainly through the renal tubules, although there is much good evidence to indicate an effect on protein fixed water and a possible action by way of the antidiuretic hormone of the posterior pituitary.

The diuresis produced by the mercury shows that enough glomerular filtrate is being formed in heart failure but that tubular reabsorption is too great. A reduction in the rate of tubular reabsorption results in a satisfactory loss of water and electrolyte with improvement of the patient. After all, 150 to 250 liters of glomerular filtrate are formed every 24 hours, while all of this is reabsorbed except for one or two liters. In congestive heart failure, the per cent change in filtration rate is relatively small while the per cent change in tubular reabsorption is great. It is quite likely that the latter is of great importance in the production of the congestive failure syndrome. It is well to remember that mercurial diuretics function very well in almost any type of edema.

2. Patients with congestive heart failure show a decided impairment of NaCl excretion following intravenous injection of 24 grams of sodium chloride.[6] The injection in normal subjects was followed by an excretion of 138-169 m. eq. of sodium per 24 hours while patients with congestive failure lost only 21-32 m. eq. in the same time. Not only was there less total loss but the concentration was less. Sodium and chloride parallelled each other. A mercurial diuretic increased the sodium excretion rate from about 30 m. eq. per 24 hours to 107. The concentration also increased. These changes were not apparently due to changes in rate of glomercular filtration as the urea clearance remained unchanged by the failure.[6]

These studies unfortunately did not include a variety of non-cardiac edema states. The above findings may not be peculiar to cardiac edema.

By what mechanism congestive failure disturbs renal function is not known. The role of the hormones, adrenal cortical and antidiuretic, can only be conjectured. It is possible to formulate a fairly satisfactory theory on the basis of disturbances in their function.

The studies of Warren and Stead[7] in which they produced "congestive heart failure" by oral administration of 12 grams of NaCl per day to three patients with heart disease and on the verge of failure fails to prove a renal cause of congestive heart failure, in that there was no control group of patients with other types of edema nor has one the right to refer to such a precipitated edema as being an example of congestive heart failure. Their work casts considerable doubt on the two classical theories.

3. The studies of Starr[8] with the use of a model of the circulation failed to support the two classical concepts of congestive failure. Such non-physiologic studies cannot be taken too seriously without physiologic data of direct sort to support it. The studies of "static blood pressure" in patients with congestive heart failure and patients without failure or heart disease shortly after death showed that heart failure was associated with an increase in blood volume and venous pressure when the heart action had ceased. Starr's studies unfortunately did not include patients with various types of non-cardiac edema. Starr suggested from his studies a possible renal factor in cardiac edema.

4. Seymour et al.[9] found the inulin clearance (rate of glomerular filtration) to be normal in congestive heart failure. Phenol red clearance (rate of effective renal blood flow) was invariably less than nor-

mal. The reduction in effective renal blood flow was proportional to the decrease in cardiac output. They failed to study patients with non-cardiac edema. These observers considered the data to indicate a greater rate of tubular reabsorption than in the normal. Furthermore, their data indicate a great filtration pressure since more glomerular filtrate was formed from less blood.

Merrill et al.[10] found, by direct catheterization of the renal veins, both the inulin and diodrast clearance to be reduced in congestive failure. The per cent reduction in the rate of renal blood flow was greater than the per cent reduction in the cardiac output. These observers considered the data to indicate an increase in filtration pressure and therefore constriction of the efferent glomerular arterioles. Bioassay showed a great increase in renin in the blood of the patients with congestive heart failure. No data were collected in patients with non-cardiac edema.

5. Schemm's[5,11] method of restricting sodium chloride and forcing water or the more conventional method of restricting sodium and allowing water libidum results in improvement of congestive failure. This apparently is not associated with direct cardiac action. It is quite likely to be closely associated with renal function in the maintenance of electrolyte balance and isotonic extracellular fluids.

SUMMARY

The above data only show the need for more studies of the mechanism and physiologic state of congestive failure. In fact, it is very unlikely that patients have ever been studied during the period that the disturbances actually responsible for the syndrome were at work. It is quite likely that these disturbances are at work for only a few seconds or heart beats and only the resultant changes have been studied to date. Furthermore, when it is realized that over 4000 liters of water leave the blood stream and return from the tissues every 24 hours, it is easily visualized how subtle the changes can be and still result in the clinical syndrome. The present day methods are not sensitive enough to measure the changes that would be involved under such circumstances.

It is safe to conclude that the mechanism of congestive heart failure is unknown and a syndrome so common as this deserves greater research attention.

REFERENCES

1. Harrison, T.: Failure of the Circulation, Williams and Wilkins Co., Baltimore, 1935.

2. McMichael, J.: The output of the heart in congestive failure, Quart. J. Med., 7:331, 1938.

3. Starr, I., Jeffers, W. A., and Meade, R. H., Jr.: The absence of conspicuous increments of venous pressure after severe damage to the right ventricle of the dog with a discussion of the relation between clinical congestive failure and heart disease, Am. Ht. J., 26:291, 1943.

4. Goodof, I. I., and Mac Bryde, C. M.: Heart failure in Addison's disease with myocardial change of potassium deficiency, J. Clin. Endocrinol, 4:30, 1944.

5. Schemm, F. R.: A high fluid intake in the management of edema, especially cardiac edema, Ann. Int. Med., 17:952, 1942.

6. Futcher, P., and Schroeder, H. A.: Studies on congestive heart failure. II. Impaired renal excretion of sodium chloride, Am. J. Med. Sci., 204:52, 1942.

7. Warren, J. V., and Stead, E. A., Jr.: Fluid dynamics in chronic congestive heart failure, Arch. Int. Med., 73:138, 1944.

8. Starr, I., and Rawson, A. J.: Role of the "static blood pressure" in abnormal increments of venous pressure especially in heart failure, Am. J. Med. Sci., 199:27, 1940.

9. Seymour, W. B., Pritchard, W. H., Longley, L. P., and Hayman, J. M.: Cardiac output, blood and interstitial fluid volumes, total circulating serum protein, and kidney function during cardiac failure and after improvement, J. Clin. Invest., 21:229, 1942.

10. Merrill, A. J., and Brannon, E. S.: Renal studies in congestive heart failure: the role of renin. Program, Southern Section Am. Federation Clin. Research, December 8, 1945.

11. Schemm, F. R.: A high fluid intake in the management of edema, especially cardiac edema. II. Clinical observations and data, Ann. Int. Med., 21:937, 1944.

NEW ORLEANS
Medical and Surgical Journal
Established 1884

Published by the Louisiana State Medical Society under the jurisdiction of the following named Journal Committee:

Rhett McMahon, M. D., Ex officio
C. Grenes Cole, M. D.
Sam Hobson, M. D.
C. M. Horton, M. D.
E. L. Leckert, M. D.
Leon J. Menville, M. D.

EDITORIAL STAFF

John H. Musser, M. D.....*Editor-in-Chief*
Willard R. Wirth, M. D.....*Editor*
Max M. Green, M. D.....*Associate Editor*

COLLABORATORS—COUNCILORS

Edwin L. Zander, M. D.
J. T. O'Ferrall, M. D.
Guy R. Jones, M. D.
T. B. Tooke, Sr., M. D.
John Snelling, M. D.
W. E. Barker, Jr., M. D.
C. A. Martin, M. D.
O. B. Owens, M. D.

Paul T. Talbot, M. D.....*General Manager*
1430 Tulane Avenue

SUBSCRIPTION TERMS: $3.00 per year in advance, postage paid, for the United States; $3.50 per year for all foreign countries belonging to the Postal Union.

News material for publication should be received not later than the eighteenth of the month preceding publication. Orders for reprints must be sent in duplicate when returning galley proof.

Manuscripts should be addressed to the Editor.

THE JOURNAL *does not hold itself responsible for statements made by any contributor.*

THE ARMY DOCTORS

There is undoubtedly a feeling amongst the doctors who sacrificed everything to go into the army and navy to help their country during the last great war that their services have not been entirely appreciated. They feel that the difficulties that have arisen in attempting to get their former practices established have been indeed great and that not much sympathy has been given to them in their endeavors nor has there been entirely a true appreciation of their unselfish call to duty.

It is hard to convince many medical officers that we who stayed at home do, with all our heart, feel grateful to them for what they have done. All this is apropos of the celebration of the 157th anniversary of the establishment of the medical department of the U. S. Army when General Eisenhower, in a coast to coast radio broadcast, praised the medical department for its great successes before and during World War II.

Another appreciation of the army medical services which were rendered practically entirely by the volunteer practicing physicians of this country is a recent editorial in Collier's, for August 3, written by Dr. Louis I. Dublin, entitled, "The Medics in World War II."

We think that this editorial in Collier's also proves that we are indeed thankful to the doctors for what they have done. The editorial is well worth reproducing.

"Casualty and disease statistics on World War II have been pretty well rounded up and collated now; and out of the statistical picture the U. S. medical profession emerges with what can only be described as glory. This applies particularly to the physicians who went to the war and took care of the wounded and dying.

"Our combat deaths, according to the Metropolitan Life Insurance Company's latest estimate, amounted to a little more than 300,000. Up to V-J Day our deaths from disease came to about 20,000, or 1-15th of the combat total.

"This was in striking and consoling contrast to our experiences in all previous wars. About the most harrowing reading you can find in connection with the Civil War is an occasional description of hospital filth, disease, and the miseries of the wounded, most of whom would literally have been better off dead. In the Spanish-American War, only 48 years ago, we lost about 15 times as many men from disease as we lost in combat—the exact reverse of the World War II ratio. In World War I, only 28 years ago, our deaths from disease totaled slightly more than those from enemy action.

"Yet in the second great war, our fighting forces were flung much farther afield

and into more fearful and wonderful climates than they had encountered in any of our other wars. They fought through malarial jungles in the South and Southwest Pacific, through filthy North African towns and rural areas, and in many a country or on many an island where sanitation was felt by the natives to be just a rather dull joke.

"Yet so highly organized and generously supplied were our medical services, and so devoted were our doctors and nurses in the field, that disease and infection were cut to the proportions of a minor menace. The percentage of wounded who died of their wounds, too, was reduced to the record low of 4 per cent, as contrasted with almost 8 per cent in World War I.

"There is only one moral to all this that we can think of. It is: Let's just keep pounding away at public health activities of all kinds, and at implementing the medical profession for more and faster progress in the conquest of disease. Our long zeal in these directions paid tremendous dividends in our latest war."

STATE HEALTH OFFICER

We were very much surprised to hear that Dr. David E. Brown was not reappointed as head of the State Board of Health. The state health officer is virtually a member of the governor's cabinet and it is certainly unusual that a recommendation made by the governor for that particular position is not approved by the senate. The only explanation that has been offered is that politics were eminently concerned with this appointment. No criticism has been made of Dr. Brown as a state health officer and certainly he has gotten along well for the most part with the medical profession in the state. It may be true that occasionally a minor difference of opinion arose between Dr. Brown and individual physicians but on the whole his tenure of office has been marked by a desire on his part to cooperate with the medical profession. It seems a remarkable thing that a man who has proved himself and has shown that he is capable of conducting a state health department should be turned down because a few senators have gotten together and have agreed among themselves that certain reappointments should not be made. It seems that there was a block who decided that they would not recommend certain of Governor Davis' appointments. As far as we can learn there were only two or three senators opposed to Brown but their feeling was that if they would in turn agree not to vote for the approval of someone else that they could block the appointment of an efficient state health officer. This was apparently accomplished. It seems like awfully picayunish and petty politics. Dr. Brown should be commended on not being amenable to pressure on the appointment of someone to a minor position who apparently was not qualified but yet had the good fortune to be a relative of a senator.

The State Board of Health definitely should be out of politics. The importance of politics in this position may be exemplified by the fact that the previous incumbent to the office was willing to give up his position, in fact he became desirous of doing so in order that he might qualify under civil service regulations and be assured of his future in the State Board of Health.

It is indeed fortunate that there was available a man in the Department who was well qualified and who will be an excellent state health officer but he, who is a career man in public health, may feel before long that political pressure may be such that it would be better for him to be under civil service than to head this important department.

By far the most important implication is the fact that the medical profession of the state of Louisiana does not have an active role in the appointment of the state health officer. The state health officer should be appointed on the basis of a recommendation or recommendations by the State Medical Society. Certainly in our two neighboring states whose health officers have been outstanding, maintenance of their position has depended entirely on the medical profession. The late Dr. Baker of Alabama who was appointed and kept in office by the

State Medical Society, is representative. Dr. Underwood of Mississippi, one of the best known health officers in the country, likewise has had a long tenure because of the state medical profession and their whole-hearted backing-up of this gentleman.

The Louisiana State Medical Society should have a definite say as to who is to be the state health officer and should have more power than they have in important medical appointments.

THE SYMPOSIUM

In this number of the Journal there is being published a symposium on salt and water balance. The papers that appear in this symposium are somewhat unusual for the Journal. It is not as a general rule that this type of presentation is published, however it is felt that the physician who has the time and the inclination to read the papers that appear in the symposium will derive much information, which is up to the moment from the laboratory and clinical studies of body fluids which have been made in recent months and years. The papers may seem too scientific for a journal essentially clinical but the reader must bear in mind that there are extremely important clinical implications in these presentations. Edema is a common symptom; it is discussed in its relation to salt metabolism. The use of diuretics is stressed and there is presented a discussion of the hormone control of water and salt. Of course of extreme importance to the doctor is the relationship of heart failure to clinical edema and renal excretion of salt and water. The fundamental knowledge of these data will do much to enable the doctor to treat his patient with a clear understanding of the purposes and the mechanism concerned when he outlines the course of therapy for the edematous patient.

ORGANIZATION SECTION

The Executive Committee dedicates this section to the members of the Louisiana State Medical Society, feeling that a proper discussion of salient issues will contribute to the understanding and fortification of our Society.

An informed profession should be a wise one.

MESSAGE FROM THE PRESIDENT

The most important activity of organized medicine at this time is to continue the fight against the Wagner-Murray-Dingell bills and similar legislation tending toward socialization of medicine. Although S.1606 did not come out of committee at the last session of Congress hearings will no doubt be continued at the next session or a third edition of the bills presented. It is thought that the medical profession at this time should take advantage of the lull and prepare for the next fight which is sure to come. Among the aims here should be to educate the public as to the views of the medical profession on such bills and to establish a better relationship with the public informing them of the results of such legislation to the medical profession and to the general public. It is felt that this should be one of the main objectives of the State Society at this time.

Special announcement concerning plans for prepayment medical service is included in this section of the Journal. It is hoped now that such a service may be put into effect by October 1. Dr. O. B. Owens and his committee have been directing their efforts to this accomplishment and we feel reasonably certain that plans will be completed by that time.

A third project before the organization is to effect a program for medical service to veterans in cooperation with the Veterans Administration, whereby the veterans may obtain medical care in their home communities by home-town doctors. Detailed plans for such service will possibly be completed within a very short time and all members of the Society will be appropriately notified

concerning regulations for participation in the plan.

Efforts are being made by the present administration to improve the scientific program for the annual meeting so that every member wil be given a worthwhile reason for attending the meeting next year. Many suggestions have been considered and announcement will be made when details have been worked out.

If these four activities—(1) defeat of bills advocating socialization of medicine; (2) prepayment medical service; (3) medical service for veterans; (4) improved scientific programs—are consummated it is felt that the present administration will have some claim of having been moderately successful.

—o—

LOUISIANA PHYSICIANS SERVICE ORGANIZED

The organization of a voluntary prepayment surgical and obstetrical care plan insurance company in the State of Louisiana is announced by Dr. Rhett McMahon, President of the State Society. The new company, sponsored by the Louisiana State Medical Society, was incorporated August 18, 1946 and is known as the Louisiana Physicians Service, Inc., and will operate on a statewide basis.

Louisiana Physicians Service is designed primarily to relieve the family of average means, particularly those of the low income group, from financial distress that frequently accompanies prolonged or catastrophic illness, but it is also available to the more fortunate as an attractive investment and a convenience.

Participation is voluntary. It leaves unaltered the established custom in the practice of medicine and in no way interferes with the individual's selection of a physician. Louisiana Physicians Service is a nonprofit mutual corporation organized by the doctors of the State of Louisiana and dedicated to the people of the State of Louisiana.

The organization of the company is the result of over two years' work by members of the Louisiana State Medical Society's Committee on Prepayment Medical Service, with Dr. O. B. Owens, Chairman.

Appointed to represent the Louisiana State Medical Society on the Board of Trustees are the following: Drs. Rhett McMahon, Baton Rouge; O. B. Owens, Alexandria; Wm. L. Bendel and George Wright, Monroe; H. Whitney Boggs, J. P. Sanders and M. D. Hargrove, Shreveport; A. V. Friedrichs, E. L. Zander, Val H. Fuchs, P. T. Talbot and Gilbert C. Anderson, New Orleans; U. S. Hargrove, Baton Rouge; W. P. D. Tilly, New Iberia; C. M. Horton, Franklin; and J. W. Faulk, Crowley.

Members of the new organization's Board of Directors are Drs. O. B. Owens, H. Whitney Boggs, Wm. L. Bendel, U. S. Hargrove, C. M. Horton, J. S. Faulk, E. L. Zander and Val H. Fuchs with Drs. Rhett McMahon and Gilbert C. Anderson as ex-officio members.

Dr. O. B. Owens was elected President of the newly organized company and Dr. Wm. L. Bendel, Vice-President, Dr. H. Whitney Boggs, Secretary-Treasurer and Frank Lais, Jr., Executive Director, compose the other officers.

All doctors of medicine licensed by the Louisiana State Board of Medical Examiners are invited to become participating physicians in the plan.

Louisiana Physicians Service does not contract to provide medical care nor may a participating physician be compelled to perform his services in any way differing from usual custom, except that the participating physician agrees to accept the fees in the Schedule of Benefits, as approved by the Louisiana State Medical Society, as full payment for service rendered after determining with the subscriber that his yearly income does not exceed $1,800 if single or $2,400 if carrying a family membership.

There is no "red tape" attached to the physician's request for payment for services rendered and the physician is assured of receiving his fees under the plan, particularly fees due from members of the low income group.

The physician will make his usual charge to patients in the "indemnity" classifica-

tion as distinguished from the members of the low income group. Patients in the higher income group will pay that portion of the fee, if any, that remains after payment has been made as an indemnity by the company to the physician.

There are some fifty-three plans, ranging from local to statewide, in operation at the present time. The total enrollment exceeds 2,800,000 persons. The number of units and subscribers has been growing since 1939. So far this year, doctor-endorsed plans have been introduced in eight states.

The recent spread has coincided with a controversy over methods of handling the problem of paying doctors' bills. President Truman has proposed a national system of compulsory prepaid health insurance to cover the cost of medical, dental, surgical and hospital care. The American Medical Association, contending such a setup would constitute "socialized medicine", has set out to aid the development of voluntary, prepayment plans sponsored and approved by state and local medical societies.

It is expected the Louisiana plan will begin operation on October 1, 1946. Doctors throughout the state will subsequently be contacted relative to their participation in the plan.

MEDICAL SERVICE COUNCIL NAMED

The appointment of Dr. A. V. Friedrichs, chairman; Dr. O. B. Owens, Dr. U. S. Hargrove, Dr. John G. Snelling and Dr. P. T. Talbot as members of the Council on Medical Service and Public Relations in the Louisiana State Medical Society was announced recently by Dr. Rhett McMahon, President of the Louisiana State Medical Society.

Frank Lais, Jr., has been named as the council's Executive Director.

TRANSACTIONS OF ORLEANS PARISH MEDICAL SOCIETY

Sept. 11. Clinico - pathologic Conference, Marine Hospital, 7:30 p. m.

Sept. 12. Clinico - pathologic Conference, Touro Infirmary, 12 noon.

Sept. 18. The Orleans Society of X-Ray Technicians, 7:30 p. m.

Sept. 25. Clinico - pathologic Conference, Marine Hospital, 7:30 p. m.

Sept. 26. Clinico - pathologic Conference, Touro Infirmary, 12 noon.
DePaul Sanitarium Staff, 8 p. m.

Sept. 27. L. S. U. Faculty Club, 8 p. m.
New Orleans Hospital Dispensary for Women and Children Staff, 8 p. m.

Oct. 1. Eye, Ear, Nose and Throat Staff, 8 p. m.
Orleans Parish Radiological Society, 7:30 p. m.

Oct. 2. Mercy Hospital Staff, 8 p. m.

Oct. 3. Executive Committee, Baptist Hospital, 8 p. m.

Oct. 4. Ochsner Clinic Staff, 8:30 p. m.

Oct. 7. Board of Directors, Orleans Parish Medical Society, 8 p. m.

Oct. 8. Clinico - pathologic Conference, Marine Hospital, 7:30 p. m.

Oct. 9. Woman's Auxiliary, Orleans Club, 3 p. m.
Touro Infirmary Staff, 8 p. m.
Clinico-pathologic Conference, Touro Infirmary, 12 noon.

Oct. 14. Scientific meeting, Orleans Parish Medical Society, 8 p. m.

Every Wednesday, Medical Discussions, Radio Station WDSU (1280 on your dial).

MAX M. GREEN, M.D., Secy.

Dr. Charles J. Bloom recently addressed a meeting of the Pike County Medical Society in McComb; his subject was "Rheumatic Fever." On July 3 Dr. Bloom was the guest speaker at a meeting of the Gulf Coast Medical Society in Biloxi; he spoke on "Recent Progress in Pediatric Treatment."

At present Dr. Bloom is in Saluda, North Carolina, teaching at the Southern Pediatric Seminar.

Drs. Joseph A. Danna, Val Fuchs, and C. Walter Mattingly were recently appointed as a medical advisory committee to the American Red Cross. Dr. Danna will serve as chairman of the committee.

Dr. F. L. Jaubert recently addressed the conference of the National Foundation for Infantile Paralysis on the problem of crippled children in the state of Louisiana.

Dr. Edward W. Nelson recently presented a paper on "Phlebothrombosis and Thrombophlebitis in Obstetrics and Gynecology" at the Rapides Parish Medical Society in Alexandria. Following the presentation a colored movie outlining the technics of vena cava ligation was shown.

At a recent meeting of the Seventh Congressional District Medical Society in Jennings, Dr. H. Randolph Unsworth gave a paper on "Psychosomatic Medicine" and Dr. Samuel B. Nadler spoke on "Surgical and Nonsurgical Jaundice."

Dr. G. J. von Langermann was elected treasurer of the Altrusa Club at a meeting of this organization held July 17.

WELCOME HOME

The following physicians were recently separated from military service: Louis J. Bristow, Jr., Baptist Hospital; Richard Buck, Audubon Bldg.; Mercer G. Lynch, Maison Blanche Bldg.; Hardee Bethea, 1007 American Bank Bldg.; M. Lyon Stadiem, 1201 Canal Bldg., Roy H. Turner, 1430 Tulane Ave.; Maurice W. Geldert, Jr., Southern Baptist Hospital.

CALLED TO MILITARY SERVICE

The following intern members were recently called to military service: Hiram W. K. Batson, Richard A. Faust, George E. McCaskey, William L. McLeod, Joseph L. Rosenzweig, George T. Schneider, William H. Syll, Gerald N. Weiss, and Earl E. Wilkinson.

CHANGES IN MEMBERSHIP ROLLS

During the month of July the following changes took place in our membership rolls:

Three physicians were transferred to the active membership rolls: Drs. Robert B. Haspel and Horace L. Wolf, former intern members, and George D. Berkett, formerly an associate member.

Five physicians removed from New Orleans and were removed from the rolls—Drs. Robert M. Rose (active), Arthur A. Calix, Eugene Hesdorffer, Pedro Suau (intern), and Harry C. Knight (associate).

CHANGES OF ADDRESS

Dr. Luis R. Oms, 505 Legendre Bldg.; Albert Segaloff, Ochsner Clinic; Wm. H. Block, 619 St. Philip St.; Dr. Henry D. Ogden, 1706 Pere Marquette Bldg.; W. P. Bradburn, Muir Bradburn, W. R. Brewster, R. J. Christman, Hyman L. Cohen, Paul McIlhenney, 1326 Foucher St.

RADIO PROGRAM

The following "Health Discussion" will be broadcast over radio station WDSU (1280 on your dial) during the month:

August 14—Eye Strain—Dr. John B. Gooch and Mr. Joseph M. Fallo.

August 21—Complications of the Diabetes Mellitus—Drs. Robert A. Katz and Mr. Fred R. Wulff, Jr.

August 28—Medical Ethics—Dr. Val Fuchs.

September 4—Prepayment Medical Plans—Mr. Edward Groner.

HANDY LITERATURE FILE

A sturdy cloth-bound literature filing box is being presented to all physicians by Schering Corp. of Bloomfield and Union, N. J.

Through direct mail, the physician receives many scientific folders designed to keep him well informed on the latest developments in the pharmaceutical field. Many physicians have desired a file box to preserve this valuable literature for ready reference. Designed to simulate a technical reference text and bound in red-purple cloth and stamped in gold, the handy file boxes are presented free of charge as another Schering service to physicians.

MEDICAL TOASTMASTERS

The Medical Toastmasters have adjourned for the summer. They will resume classes in the fall.

During this recess a canvass of the membership of the Society will be made to secure new members.

As previously mentioned these classes are held to improve one's oratorical ability. Dale Carnegie's textbook on public speaking is the basis of teaching; there are sixteen lectures in all. Each member of the class is called upon to give a three-minute talk, and is quizzed on certain sections of the night's lecture.

It has been suggested that when classes resume they be held in the Hutchinson Memorial Auditorium, 1430 Tulane Avenue, at 8 or 8:30 p. m., rather than having a dinner meeting at 6:30 p. m. at the New Orleans Athletic Club.

Another suggestion that has been made is that an English professor or a director of public speaking at one of the high schools or universities be engaged to correct delivery, diction, etc.

If you are interested in participating in these classes you are urged to communicate with Dr. Edwin L. Zander, president of the Medical Toastmasters, or Dr. L. J. O'Neil, the secretary, as there is a limit to the number of members that these classes may accommodate.

LOUISIANA STATE MEDICAL SOCIETY NEWS

CALENDAR

PARISH AND DISTRICT MEDICAL SOCIETY MEETINGS

Society	Date	Place
East Baton Rouge	Second Wednesday of every month	Baton Rouge
Morehouse	Second Tuesday of every month	Bastrop
Orleans	Second Monday of every month	New Orleans
Ouachita	First Thursday of very month	Monroe
Rapides	First Monday of every month	Alexandria
Sabine	First Wednesday of every month	
Second District	Third Thursday of every month	
Shreveport	First Tuesday of every month	Shreveport
Vernon	First Thursday of every month	

ATTENDANTS AT A. M. A. MEETING

The following members of the State Medical Society attended the annual meeting of the American Medical Association which was recently held in San Francisco. From New Orleans:

Drs. Hartwig M. Adler, Ansel M. Caine, Curtis W. Caine, Charles L. Cox, Jules Myron Davidson, M. E. DeBakey, Thomas Findley, Warren Hebert, J. C. Henthorne, M. O. Hines, James K. Howles, Edgar Hull, Robert A. Katz, Maurice Lescale, Wilkes A. Knolle, Alton Ochsner, Walter J. Otis, Cassius L. Peacock, Ralph V. Platou, P. J. Saleeby, John H. Seabury, Daniel N. Silverman, Roy H. Turner, Woodard D. Beacham, George E. Burch, Guillermo M. Carrera, Boni J. DeLaureal, Emma S. Moss, William Parson, John C. Weed, B. Bernard Weinstein, Monroe Wolf, John Adriani, Donovan C. Browne, Eugene B. Vickery, E. Carroll Faust, and Champ Lyons.

From elsewhere in the state: Drs. W. P. Butler, A. A. Herold, C. P. Rutledge, J. D. Talbot, Shreveport; Drs. H. O. Barker, L. D. Gremillion, O. B. Owens, Alexandria; Dr. J. Q. Graves, Monroe; Dr. L. H. Lafargue, Sulphur; Dr. D. F. Davis, Lake Providence; Dr. S. F. Fraser, Many; Dr. H. M. Prothro, Pleasant Hill.

TULANE FACULTY MEMBERS COMMENDED

Six members of the faculty of the Tulane Medical School and one former member have been commended by the O.S.R.C. in conjunction with researches they carried out in cooperation with or at the suggestion of this committee. The members to be commended are Dr. Ernest Carroll Faust, professor of parasitology; Dr. Ralph G. Smith, professor of pharmacology; Dr. R. V. Platou, professor of pediatrics; Dr. Alton Ochsner, professor of surgery; Dr. Guy A. Caldwell, professor of orthopedics; Dr. George E. Burch, associate professor of clinical and experimental medicine, and Dr. Walter J. Horton, former assistant professor of chemistry, now head of the department of chemistry at the University of Kansas.

CONSULTANTS TO THE SECRETARY OF WAR

The Office of The Surgeon General announces the appointment of medical consultants throughout the United States. The following men have been selected from the south: Dr. Walter B. Martin, Norfolk, Va.; Dr. John Minor, Washington, D. C.; Dr. Henry M. Thomas, Jr., Baltimore, Md.; Dr. Roy H. Turner, New Orleans, La.; Dr. Wm. T. Rainey, Fayetteville, N. C.; Dr. Virgil P. Sydenstricker, Augusta, Ga.

MISSISSIPPI VALLEY MEDICAL SOCIETY

This organization will meet at the Jefferson Hotel, St. Louis, on September 25-27. A distinguished list of guest speakers have consented to appear on the program.

NEW JOURNAL OF DERMATOLOGY AND SYPHILOLOGY

The publication of a new journal on dermatology and syphilology, the Quarterly Review of Dermatology and Syphilology, has been announced by the Washington Institute of Medicine. The Editor-in-Chief of this new journal will be Donald M. Pillsbury with Herman Beerman and Clarence S. Livingood, associate editors.

AMERICAN BOARD OF OBSTETRICS AND GYNECOLOGY

The next written examination (Part I) will be held on Friday, February 2, 1947. As a number of changes in Board regulations and requirements were made effective at the last annual meeting of the Board held last May, it would be advisable for candidates for licensure to communicate with Dr. Paul Titus, Secretary, 1015 Highland Building, Pittsburgh 6, Pennsylvania.

AMERICAN HOSPITAL ASSOCIATION

Rear Admiral Dallas G. Sutton (MC) USN (Rt.) comes to the Washington Service Bureau staff of the American Hospital Association on September 1 as director of study of government hospital relations. Admiral Sutton will serve as a

liaison between the association and the federal government in matters concerning the federal hospital program and will assist in the coordination of civilian and federal hospital facilities.

Among Admiral Sutton's more recent assignments was that of Assistant Surgeon General, 1937 to 1941. During 1941 and early 1942 he was commanding officer of the Naval Hospital, Portsmouth, Virginia, after which he was in charge of construction of the Naval Medical Center at Bethesda, Maryland, erected the same year. From that time until his retirement in April of this year, Admiral Sutton was inspector of all east coast activities of the Naval Medical Department.

NEWS ITEMS

The seventh Annual Congress on Industrial Health sponsored by the Council on Industrial Health of the A. M. A. will be held at the Copley-Plaza Hotel, Boston, Massachusetts, September 30-October 2.

The National Society for the Prevention of Blindness will hold a three day conference at the Hotel Pennsylvania, New York, November 25-27.

Colonel Frank S. Gillespie of the Royal Army Medical Corps was presented the Legion of Merit by General Eisenhower. Innumerable medical men have had the opportunity of meeting and knowing Dr. Gillespie who served for some four years as British Medical Liaison Officer in the Army Medical Department.

NURSES FOR POLIOMYELITIS

On account of the marked increase in number of cases of poliomyelitis this year there is a dearth of nurses to take care of these children. The Red Cross is preparing to recruit nurses to be paid by the National Foundation for Infantile Paralysis in the states in which the disease is particularly rife. Louisiana is one of 11 states which requires additional nursing help.

PHYSICIAN WANTED

A cooperative insurance group recently organized in Pollock, Louisiana is desirous of securing services of a doctor; salary $200-$300 per month, office furnished. Outside general practice available.

For further information contact Mr. W. E. Groves, 420 Audubon Building, New Orleans. Telephone Ra. 6093.

TWENTY-FIFTH ANNIVERSARY OF THE DISCOVERY OF INSULIN

The twenty-fifth anniversary of the discovery of Insulin will be observed with a program in Convocation Hall, at the University of Toronto, on September 16. Many internationally known figures in the field of medicine will be present to honor the occasion. Among them will be R. D. Lawrence, physician in charge, Diabetic Clinic, Kings College Hospital, London, England; H. C. Hagedorn, of Gentofte, Denmark; Bernardo A. Houssay, Research Institute of Experimental Biology and Medicine, Buenos Aires, Argentina; and Elliott P. Joslin, Harvard Medical School, Boston, U. S. A. This observation will be followed by the regular annual meeting of the American Diabetes Association.

On September 23, Eli Lilly and Company will sponsor an International diabetes clinic to be held at the Indiana University Medical Center in Herty Hall of the State Board of Health Building, Indianapolis, Indiana. International importance will be given to this meeting by the presence of Professor Charles H. Best, Toronto, Canada, co-discoverer with Banting of Insulin, Professor Houssay, Dr. Lawrence, and Dr. Hagedorn. They will discuss various phases of diabetic care.

HEALTH IN NEW ORLEANS

The Bureau of the Census, Department of Commerce reported that for the week ending July 13 there were 148 deaths in the City of New Orleans, as contrasted with 106 the previous week. These deaths were divided 103 white, 45 non-white, with 27 of the total occurring in children under one year of age. For the week which came to a close on July 20 there was a considerable reduction in number of deaths of citizens of New Orleans; 124 people expired in this particular week, 80 of whom were white, 44 of whom were colored and only seven of the total being in children under one year of age. There was a slight increase in the number of deaths for the week ending July 27 but as in the past some months the number of deaths is below the three year average of the corresponding week of the year. In this particular week the 131 deaths were divided 82 white and 49 colored with 17 deaths in children under one year of age. For the week which closed August 3 the 128 deaths in the City of New Orleans were apportioned 95 white, 33 colored, with an astounding low infant mortality of only five.

INFECTIOUS DISEASES IN LOUISIANA

The weekly morbidity report for the State of Louisiana for the week ending June 29 showed measles leading all other reportable diseases with 53 cases and only three other diseases occurring in numbers greater than ten, namely, pulmonary tuberculosis with 22 cases, poliomyelitis with 13 and mumps with 11. The very large number of poliomyelitis cases were confined almost entirely to the southern parishes of the state; Lafayette Parish with four cases, Iberville with three and East Baton Rouge with two, were the parishes which had more than one case. For the week which closed July 6 the following diseases occurred in numbers greater than ten; cancer 173, unclassi-

fied pneumonia 114, measles 57, mumps 50, malaria 45, rheumatic fever 35, pneumococcic pneumonia 33, chickenpox 28, septic sore throat 19, whooping cough 17, influenza 15, poliomyelitis 14, amebiasis 13 and hookworm infestation ten. Again, the poliomyelitis cases were found to have occurred largely in the southern parishes, Orleans and Vermilion with three each, were the only two parishes which had a greater number than one case. All of the malaria cases were contracted within the Continental United States. For the week which closed July 13 pulmonary tuberculosis was reported in 78 instances, followed by 18 cases of poliomyelitis, 14 of typhus fever, 12 of unclassified pneumonia and ten of measles. The poliomyelitis cases, except for two reported from Caddo and one from Ouachita, were again confined to the parishes in the southern portion of the state.

Indicative of the presence of poliomyelitis is the fact that for the week ending July 20 it was second in the list of reportable diseases, with 27 cases, preceded by pulmonary tuberculosis only, with 29 cases. Other diseases in numbers greater than ten included 20 cases each of malaria and typhus fever, 17 of diphtheria, 11 each of measles and typhoid fever and ten of scarlet fever. The poliomyelitis cases were reported in greatest number in Ouachita Parish with five instances, followed by Orleans Parish with three, Caddo with two and East Baton Rouge with two. Other reported cases were found in numbers no greater than one in various parishes throughout the state. For the week ending July 27 there were listed 44 cases of pulmonary tuberculosis, 35 of measles, 18 each of poliomyelitis and of whooping cough, 15 of unclassified pneumonia, 13 each of septic sore throat and influenza and 11 of mumps. There was a reduction in the number of cases of poliomyelitis reported this week but the number is still large. So far up to date this year 148 patients with poliomyelitis have been reported to the State Board of Health. Of the 18 cases this week no one parish had more than two originating within its borders.

MONTHLY MORBIDITY FOR VENEREAL DISEASES STATE OF LOUISIANA

Month Ending June 30, 1946

	Total This Month	Total Previous Months	Total To Date 1946
Chancroid	54	284	338
Gonorrhea	1345	8837	10182
Granuloma inguinale	25	143	168
Lymphopathia venereum	12	55	67
Syphilis	1651	8402	10053

PHARMACOPEIA REVISION

Many requests have been received by the Committee on Revision of the Pharmacopeia of the United States of America relative to the deletions which will be made in the U.S.P. XIII of titles representing items which were official in the U.S.P. XII. The list of drugs omitted is as follows:

Acetonum
Acidum Aceticum
Acidum Aminoaceticum
Acidum Lacticum
Acidum Mandelicum
Acidum Nitricum
Acidum Phosphoricum
Acidum Phosphoricum Dilutum
Acidum Sulfuricum
Acidum Sulfuricum Dilutum
Aethylis Chaulmoogras
Alcohol Dehydratum
Allylis Isothiocyanas
Althaea
Antipyrina
Aqua Chloroformi
Argentum Proteinicum Forte
Belladonnae Radix
Bismuthi Subnitras
Calcii Phosphas Tribasicus
Capsulae Carbonei Tetrachloridi
Capsulae Olei Chenopodii
Capsulae Triasyni B Cum Hepati
Carbonei Tetrachloridum
Ceratum
Ceratum Resinae
Chloramina-T
Codeina
Colchici Semen
Concentratum B-Vitaminarum Hepatis
Decocta
Emplastrum Belladonnae
Emulsum Olei Terebinthinae
Ergota
Eriodictyon
Eucainae Hydrochloridum
Extractum Hyoscyami
Extractum Malti
Extractum Rhei
Fel Bovis
Ferri Et Ammonii Citrates Virides
Ferrum Reductum
Fluidextractum Ergotae
Fluidextractum Eirodictyi
Hydrargyri Bichloridum
Hydrargyri Salicylas
Hydrargyri Succinimidum
Hydrargyrum cum Creta
Infusa
Injectio B-Vitaminarum Hepatis
Injectio Hydrargyri Salicylatis
Injectio Strophanthini
Injectio Triasyni B cum Hepati
Linum
Liquor Acidi Arseniosi
Liquor Hydrogenii Peroxidi Fortior
Liquor Iodi
Lycopodium

Magnesii Phosphas Tribasicus
Massa Ferri Carbonatis
Mel
Nux Vomica
Oleum Amygdalae Amarae
Oleum Chaulmoograe
Oleum Chenopodii
Oleum Juniperi
Oleum Lini
Oleum Picis Rectificatum
Oleum Pini Pumilionis
Oleum Terebinthinae
Oleum Terebinthinae Rectificatum
Pamaquinae Maphthoas
Pelletierinae Tannas
Phenylis Salicylas
Pilulae Ferri Carbonatis
Potassa Sulfurata
Potassii Bitartras
Potasii Nitras
Pulvis Cretae Compositus
Quininae Aethylcarbonas
Quininae et Ureae Hydrochloridum
Resina
Serum Antimeningococcicum
Serum Immune Morbillosi Humanum
Serum Immune Scarlatinae Humanum
Sevum Praeparatum
Sodii Cacodylas
Spiritus Anisi
Spiritus Camphorae
Spiritus Frumenti
Spiritus Glycerylis Trinitratis
Spiritus Vini Vitis
Strophanthinum
Sulfapyridinum
Sulfapyridinum Sodicum Sterile
Syrupus Picis Pini
Tabellae Magnesii Phosphatis Tribasici
Tabellae Sulfapyridini
Terpini Hydras
Thymolis Iodidum
Tinctura Colchici Seminis
Tinctura Lodi (7 per cent)
Tinctura Nucis Vomicae
Toxitabellae Hydrargyri Bichloridi Magnae
Toxitabellae Hydrargyri Bichloridi Parvae
Trinitrophenol
Unguentum Iodi
Zinci Acetas
Zinci Chloridum

THE FEDERAL COMMUNICATION COMMISSION AND ITS PROPOSED ACTION ON DIATHERMY INTERFERENCE

The Federal Communication Commission is an attempt to prevent interference to F. M. and Television Broadcasting by diathermy or other electronic equipment of the non-radio category, is setting up certain standards of good engineering practice to be observed by manufacturers of this type equipment.

They intend to set certain frequencies of operation and tolerances for such equipment, and issue certificates to the manufacturer of the equipment, if their equipment passes certain required tests.

The requirements do not mean that the doctor has to discard his present equipment. However, he can satisfy himself as to what can be done to help him in the following manner.

Register his diathermy with some good service organization—preferably one which specializes in his type of equipment. The service shop will inform him as to practicability and cost of making the diathermy meet the specifications.

If the doctor purchases new equipment, obtain from the seller a money back warranty that the diathermy meets the F C C requirements and that the manufacturer is cooperating with the F C C in adapting good standards to such equipment.

As far as present equipment is concerned, it is not necessary to trade in or otherwise dispose of perfectly good equipment. It may happen that the diathermy meets all requirements, or is far enough away from Radio Equipment so that it does not cause interference.

References:

"Diathermy Standards"
Electronic Industries, July 1946, p. 151

Federal Communications Commission
Public Notice 84900, Sept. 25, 1945
also 71021 Oct. 5, 1943
also News Release 85742, Oct. 23, 1945

BOOK REVIEWS

The Principal Nervous Pathways: By A. T. Rasmussen, Ph. D. New York, The Macmillan Company, 3rd ed., 1945. Pp. x + 73, figs. 28. Price, $3.50.

First published in 1932, this useful series of neurological charts and schemas with explanatory notes is widely and favorably known. It comprises twenty-eight plates (8 x 11 inches), chiefly representing functional pathways so drawn as to show both their anatomic relationships and the neuron chains composing them. Each plate is labeled and faced by a page or more of explanatory notes. The subjects of the plates are well chosen for their practical importance in medicine. In preparing the third edition the author has modified some of the charts of functional pathways in

accord with recently established findings. The volume is recommended, for use either as by students as an atlas supplement to a text or as an independent reference for readers who are already familiar with the general organization of the nervous system.

HAROLD CUMMINS, Ph. D.

Howell's Textbook of Physiology: Ed. by John F. Fulton, M. D. Philadelphia, W. B. Saunders Company, 1946. Pp. 1304. Price, $8.00.

Although this textbook reports to be the fifteenth edition of Howell's Textbook of Physiology, it should be emphasized that it is virtually a new contribution ably edited by Dr. Fulton with the aid of some twenty-three contributors. It differs from the majority of the recent textbooks in physiology in minimizing clinical application and in presenting the material from the point of view that physiology is an academic discipline in its own right. This does not imply, of course, that the textbook will be of no interest to the clinician. On the contrary, the latter will find it an unusually well written and valuable account of the modern concepts of modern trends and beliefs in physiology.

The first section (about 40 per cent of the book) is devoted to a comprehensive and splendidly written section on the principles of nervous and muscular activity and on the nervous system, which leaves very little to be desired. The succeeding sections on blood and circulation are not quite as successful. The authors have experimented with a novel presentation of the material, but in doing so seem to have sacrificed unity and completeness. The problems of shock and hemorrhage, for example, would seem to warrant more specific and complete treatment than that contained in the few pages devoted to these topics. On the other hand, many of the individual chapters are to be recommended. The chapter on hemodynamics is particularly well done. The remainder of the book is taken up with discussions of respiration, body fluids and kidney, digestion, and metabolism and nutrition. The final section presents an excellent discussion of the physiology of reproduction.

Of interest and perhaps the only serious criticism of this otherwise fine contribution is the fact that the authors did not include a section dealing specifically with the endocrine glands. While there are references to the thyroid, adrenal, etc. in various discussions, there is no detailed information or emphasis as to the role of the endocrine glands as the second great coordinating system of the body. The parathyroid is not even mentioned in the index.

H. S. MAYERSON, Ph. D.

A Malariologist in Many Lands: By Marshall A. Barber, with a Foreword by Paul F. Russell, Lawrence, Kansas, Univ. of Kansas Press, 1946. Pp. 158. 7 pl. of photo. Price, $2.50.

This is a most entertaining and informative little book, of interest to malariologists, physicians and to laymen who are interested in the main highways and some of the by-ways of development of knowledge in the field of malaria, together with methods for its diagnosis and control.

Although Dr. Barber first became acquainted with malaria parasites of man a half century ago while a junior instructor at the University of Kansas (at a time when malaria was still present in that state), his intensive study of the parasite and the syndromes which it produces began in 1920 when he joined the U. S. Public Health Service. His intensive blood-film and spleen surveys, as well as anopheline-host transmission studies in the Southern United States were followed by similar undertakings in Tropical America, the Philippines, Malaya, the Fiji Islands, Equatorial Africa, Egypt, Macedonia, Cyprus, Turkey, the U.S.S.R. and India. In addition to accumulating a wealth of epidemiological data, Dr. Barber will be known for three particular contributions in malaria, namely (1) thick-blood films for diagnosis of the malaria parasites, (2) introduction of Paris green as a larvicidal agent for control of anopheline mosquitoes and (3) demonstration that plasmoquin as a therapeutic agent in human malaria sterilizes the circulating gametocytes, so that susceptible mosquitoes taking blood meals from human cases do not become infected. It may be of interest to add parenthetically that before 1920 Dr. Barber had developed the micro-manipulator for isolation of individual bacteria, and that he demonstrated this to the astonishment of the great Robert Koch.

The story of Dr. Barber's adventures in the field of malariology is told in his own inimitable way, as, for example, on page 50 his statement that "when the Devil sowed malaria, he took care to supply it with plentiful and efficient vectors." The reader's attention is maintained from beginning to end. Frequently in the midst of a running narrative one suddenly finds set down valuable diagnostic technics.

The print is clean and the little volume simply but attractively bound. The introduction is by Col. Paul F. Russell, M.C., A.U.S., who is a world authority on malaria.

"A Malariologist in Many Lands" is heartily recommended to the weary physician who desires a change from the usual type of detective story.

ERNEST CARROLL FAUST, M.D.

The Modern Attack on Tuberculosis. Revised Edition: By Henry D. Chadwick, M.D.,and Alton S. Pope, M.D., Rev. Ed. New York. The Commonwealth Fund. Price, $1.00.

This small manual opens with a quotation from an address delivered by Dr. Wade H. Frost in 1935, "The eradication of tuberculosis is now an expectation sufficiently well grounded to justify shaping our tuberculosis control program toward this definite end." It concludes with a forecast: "The bells that ring in the year 2000 may sound the death knell of the tubercle bacillus." These two optimistic predictions are well supported by the collection of data presented in the six chapters of this handbook on tuberculosis control. It was the aim of the authors not to present new but rather to collect for the tuberculosis work a mass of data ordinarily disseminated throughout the medical literature.

It is interesting to see that the emphasis is placed on the individual patient with tuberculosis not as a therapeutic problem, because adequate means of therapy are available, but as a focus for preventing perpetuation of the communicable disease. The publicized increase in morbidity rates from tuberculosis among the aged is believed to be only a transient phenomenon. The sanatorium as a means of controlling tuberculosis by isolating those most likely to transmit the disease is emphasized strongly. Now that photoflourographic methods are available for progressively increasing segments of the population, the authors urge intensive "follow-up" procedures so that the unsuspected case and the contacts of known cases may be repeatedly examined. Very simply they illustrate the necessity for this. In both instances, the unsuspected case and the contact, the chances are very great that the tuberculosis will be only minimal. By way of contrast, they cite the fact that even today about 25 per cent of all patients admitted to tuberculosis sanitoria have hopelessly advanced disease.

This book is recommended to any physician who wants to understand the methods by which public health authorities hope eventually to eradicate tuberculosis.

SYDNEY JACOBS, M.D.

Cornell Conferences on Therapy, Vol. I. Ed. by Harry Gold, M.D. New York. The MacMillan Company, 1946. Pp. 322. Price, $3.25.

Therapeutic conferences may be arranged in seminar style or in one where frank differences of opinion are encouraged. The latter was the one chosen when representatives of the various clinical and pre-clinical groups of Cornell University Medical School inaugurated their conferences for medical students in 1937. Because these became so popular and soon attracted not only students and residents but also many visiting physicians, it was decided to record stenotypically everything that was said at each conference. This material has been properly edited and presented as the first volume in what should be a most interesting series.

The diversity of subjects in the first volume compels attention. From such points of departure as the contents of a doctor's bag (many doctors' bags were examined, and most held little material for rendering first-aid to the more commonly encountered emergencies in general practice) to the Rh factor, the groups of consultants exchanged opinions. The clinically useful is constantly stressed.

Regardless of how limited or how broad his clinical interests, any practitioner can learn much from reading this delightful book. The exercises in clinical thinking contained are most stimulating.

SYDNEY JACOBS, M.D.

Theory of Life, Disease and Death: By Morton Whitby. Chicago. Cutler Publishing Co. 1945. Pp. 275. Price, $5.00.

The author, a member of the Royal College of Surgeons and a fellow of the Royal Society of Medicine, has concluded that life exists only because of the electrical energy which is present in the living substance. This is the mystic power controlling inorganic or organic matter and is the "symbol of God." Death is a loss of this electrical energy, while disease results in the transfer of energy to the area of disease to the detriment of the organism as a whole. Accordingly, the measurement of the electrical pattern becomes of paramount importance. If this is done, with care and patience, by means of the Ellis Micro-Dynameter (seven U. S. patents), one can make an accurate diagnosis of disease with the help of only a few biochemical analyses. The apparatus is also invaluable in the "dynamic treatment" of disease.

In these hectic days when life and the practice of medicine have become complicated almost to the breaking point, it is reassuring to discover at least one individual who feels that much of this effort is unnecessary, and that the struggle can be resolved so simply. In face of an acute paper shortage, however, the reviewer wonders how or why this book was ever published. It may be only coincidence that it was published in Chicago where the dynameter was designed.

H. S. MAYERSON, Ph.D.

A Blind Hog's Acorns: Vignettes of the Maladies of Workers: By Carey P. McCord, M.D. (Illustrations by Francis Strobel). Chicago, Cloud, Inc., 1945. Pp. 311. Price, $2.50.

This book, a narrative autobiography of experiences in industrial hygiene, is true to the interesting type of story expected from Dr. McCord by those who know him personally or have heard him at the banquet table during meetings of industrial physicians.

The enthusiasm that Dr. McCord has put into a career of investigation and control of industrial disease registers as the experiences are recounted and the frequently ingenious solutions are given. This book will probably have its greatest appeal to those persons whose work takes them into the field of industrial hygiene. Any student of industrial hygiene would profit from these easily read accounts of industrial illnesses.

This reviewer feels that the choice of the artist who drew the illustrations might have been more happily made. Somehow the illustrations do not catch the tone of the narrative and the artist just cannot draw blind pigs.

RALPH H. HEEREN, M.D.

New Drugs: By Arthur D. Herrick, with a foreword by Dr. Austin E. Smith. 319 pages, buckram. Published by Revere Publishing Company, 11 Stone Street, New York 4, N. Y. 1946. Price, $4.00

"New Drugs" consists of a description and discussion of the legal procedures necessary before a new drug can be made available for general use. As such, it is concerned chiefly with Section 505 of the Federal Food, Drug and Cosmetic Act and with regulations under that section of the Act. It may well serve as a guide regarding the requirements and policies of enforcement of the law and consequently should be of particular interest to drug manufacturers and distributors who are directly concerned with the introduction of new drugs. Since the book is written in the light of experience with existing laws it should also be a useful guide in the enactment of similar laws by states, municipalities or by other countries. Such questions are answered as: What constitutes a new drug? What drugs are exempt? What is the procedure necessary by the distributor for application for the release of a new drug? What type of evidence must be presented to establish its safety and how may such evidence be obtained? A number of appendices make up almost half of the volume. Appendix A is the "Report of the Secretary of Agriculture on Deaths Due to Elixir Sulfanilamide," which concerns a tragedy responsible in no small part for the enactment of legislation concerning the introduction of new drugs. Appendix B is the "Federal Food, Drug, and Cosmetic Act and Regulations." Appendix C records "State and City New Drug Legislation," while Appendix D is the "Official Rules of the Council on Pharmacy and Chemistry of the American Medical Association" which have been somewhat revised since the book was written. "New Drugs" concerns a field of endeavor not usually realized by the general public but established for its protection. Even a large part of the medical profession is unfamiliar with this phase of drug control or takes it for granted. Although the information is most valuable to the manufacturer and distributor of drugs it should also be of interest to the medical profession and even to the general public.

RALPH G. SMITH, M.D.

Principles and Practice of Tropical Medicine: By L. Everard Napier, C.I.E., F.R.C.P. New York. The MacMillan Company. 1946. Pp. 917, Price, $11.00.

This new volume by Dr. Napier is a revision and an expansion of his earlier work which was reviewed in the New Orleans Medical and Surgical Journal, June 1944, p. 607. The volume now offers a complete picture, and a very satisfactory one, of tropical diseases. In the introduction, among many pertinent observations, the author warns against allowing the laboratory aspects of diagnostic methods to dominate one's thinking, which this reviewer considers most timely in the light of the mistakes he has seen made in the diagnosis of leprosy by too slavish adherence to the results of laboratory tests. The new parts of the book, making up about one-third of the total of 784 pages, covers treponema infections, skin diseases, the predominantly tropical venereal diseases, nutritional diseases and parasitic diseases. As the review referred to above covered sufficiently the contents of the earlier volume these comments will be confined to the newer parts of the work. The controversial question as to the relation of yaws and syphilis, the author resolves by regarding the causative organisms as "closely related but of quite distinct species." The author considers that both diseases "arose from a common ancestor, probably in prehistoric times." In the parallel column differentiation of the two diseases, the writer places the response to mercurial treatment as one of the features; since mercury is now rarely used in syphilis this probably is not very helpful. Penicillin is mentioned in the treatment of yaws, illustrating the pains the writer has taken to bring the book up to date. Under the discussion of prevention of tropical ulcer the writer points out the fallacies that are inherent to generalizations in fields where our knowledge is limited. To one interested especially in preventive medicine it is discouraging, but not surprising, to find that the

author expresses the opinion that ringworm of the feet is almost a concomitant of living in the tropics. The sections dealing with medical parasitology consider the diseases primarily from the point of view of the clinician but public health and epidemiological aspects are particularly competently handled. The section on nutrition and nutritional diseases in the tropics starts with general consideration of diet with special attention given to rice which is so largely eaten in warm climates. The economic factors are given adequate attention. While the author gives full credit to Goldberger for his monumental work in pellagra he feels "that no explanation of the etiology of pellagra can be accepted that does not take into consideration the past and present predominance of the disease among people whose staple food is maize." In the section on rabies there is a very good appraisal of the circumstances that should lead one to administer antirabic vaccine. The book as a whole can be recommended without reservation to students and physicians who need to learn about and to deal with diseases occurring predominantly in warm climates.

G. W. McCoy, M.D.

Proceedings of the Rudolph Virchow Medical Society. Vol. 3, 1944. New York, Brooklyn Medical Press, 1945. Pp. 104. Price, $2.00.

A volume of interesting articles on subjects, medical, surgical, roentgenologic and the specialties. The articles are brief and interesting. The size of the magazine does not justify detailed description of the contests, but anyone will find an hour of pleasant and profitable reading.

I. L. Robbins, M.D.

PUBLICATIONS RECEIVED

Commonwealth Fund, New York: Psychotherapy in General Medicine, by Geddes Smith. Medical Education and the Changing Order, by Raymond B. Allen, M.D., Ph.D.

Lea & Febiger, Philadelphia: Urologic Roentgenology, by Miley B. Wesson, M.D.